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REVIEW

An Overview of Social Participation in Older Adults: Concepts and Assessments

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ABSTRACT. In older adults, social participation is an important component of rehabilitation and health promotion. Several studies have attempted to describe the definition and concepts of social participation, and there were many outcomes to measure social participation. This overview provides information about representative social participation and related concepts that have been defined in the literature. A standardized definition of social participation has not been developed; commonly, recognition for social participation was proposed as focused on involvement in social activities that provide interaction with others in a society or community. Many instruments assess the various aspects of social participation. Because of operational definition and diversity in social participation, performance in social participation was adopted as an aspect of assessment. Further discussions are needed to clarify the definition of social participation and evaluate the instruments used to assess social participation for it to be useful for rehabilitation and health promotion. In doing so, determining and developing assessment and intervention based on the purpose or perspective of social participation in older adults with and without disabilities is important.

Key words: Social participation, Definition, Concept, Assessment

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Social participation is a modifiable health determinant for successful aging in older adults. International interest in social participation is increasing yearly[1,2)]. However, despite the interest in social participation, no standardized definition of the term exists. The International Classification of Functioning, Disability and Health (ICF) proposed by the World Health Organization (WHO) provides an internationally accepted taxonomy of functioning and disability with standard terminology and a conceptual framework of health domains for the description of health-related states[3)]. The ICF defines participation as "involvement in a life situation," participation restriction as "problems an individual may experience in involvement in life situations," and activity as "the execution of a task or action by an individual." Activity and participation are divided into a single list of nine domains[4)]. The ICF has a major impact on the use and understanding of participation in healthcare; however, some overlaps exist in the components of activity and participation. Although four alternatives have been prepared for structuring the relationship between activities and participation in terms of the ICF domain list, the WHO has also stated the difficulty in distinguishing between "activities" and "participation" based on the domains in the component[3)]. The boundary between the two dimensions in the ICF[5)] is unclear[6)]. Additionally, similar social participation concepts, expressed as synonyms and terms related to participation, social engagement, social involvement, community engagement, community involvement, and community participation, have been operationally defined and interchangeably used as social participation[6,7)]. Even the distinction between "participation" and "social participation" has not been fully clarified[8)]. The definition proposed by Levasseur et al.[7)] is a reasonable, well-organized explanation of social participation and is a well-known definition. Levas-

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seur et al.[7] performed a content analysis of 43 articles with original definitions of social participation in older adults. The authors defined social participation as "a person's involvement in social activities that provide social interactions within his/her community or society." Their content analysis showed that social participation definitions mostly focus on the involvement of a person in activities providing interactions with others in the society or community. Six proximal to distal levels of involvement of an individual with others were identified: 1) doing an activity in preparation for connecting with others, 2) being with others, 3) interacting with others without doing a specific activity, 4) doing an activity with others, 5) helping others, and 6) contributing to society (Table 1). These hierarchical levels were summarized as social participation (levels 3-6), participation (levels 1-6), and social engagement (levels 5 and 6).

Each level of social participation has several domains according to the content or context classified by the ICF. Older adults can carry out various types of social participation. Bukov et al.[9] distinguished three types of participation with respect to content, context, and resources required to participate: collective participation as "the common act of group members, whereby the intention is directed toward the group itself and not toward reaching an outside goal"; productive participation as "the rendering of services, goods, and benefits for others"; and political participation as "acts of decision-making about social groups and the allocation of resources." They reported that collective participation accounts for a large proportion of the three types of social participation among older adults aged 70 and over. Serrat et al.[1] pointed out diversity of social participation in older adults and classified social participation into four types based on two forms (individual or collective) and two participations (social or political). These social participation activities often do not necessarily originate obligatorily or unconsciously by duty. They are optionally or consciously performed according to the wishes, preference, inclination, etc. of a person in older adults. Actual social participation in older adults differs depending on their age and type of social participation[9]. Not all older adults participate or need to participate in all possible types of social participation[10,11]. In an individual's rehabilitation and health promotion, the following points seem to be important when considering meaningful participation for the person from among a number of social participations: 1) which social participation is weighted to the person, 2) what each social participation means to the person, and 3) how the meaning of interaction is included in the performance of social activities of the person. Social activities and interactions are essential elements of social participation[7]. The meaning of the interaction may be any or all the "antecedents for social participation," "a phenomenon in social participation," and "consequences caused by social participation." The performance of one social activity can be quantitatively measured; however, quantitatively showing how much the interaction, which is the essence of social participation, is included in the performance is not easy. Aspects such as the "importance" or "satisfaction" of social participation for a person may help understand how much interaction is reflected in the person in a certain social participation.

In addition, social participation through these social activities, depending on the type, is often performed in an outdoor or indoor environment. The definition of social participation includes a definition focusing on social participation in the outdoor environment. Dehi Aroogh M et al.[12] conducted a concept analysis of social participation in older people based on 57 articles published between 2000 and 2018. They defined social participation in older adults as "the conscious and active engagement in outdoor social activities leading to interacting and sharing resources with other people in the community, and the person has a personal satisfaction resulting from that engagement." Social participation is carried out not only outdoors but also indoors, and outdoor social participation has a wider environment and enriched activities; however, older adults may place importance on social participation that can be carried out indoors. Some healthy community-dwelling older adults need to participate in the family society by performing domestic roles and assisting families with disabilities. They also interact with many others through social networks by computer and mobile phone. On the other hand, older adults with disabilities tend to have a living space limited to the indoors. It is not only important to enhance activities outdoors but also indoors[13,14]. It may not always be necessary to limit the location of social participation to outdoors depending on the content and characteristics of the social participation. Determining if the participation is a priority for the person's future daily life or the kind of impact that the social participation will have on the person seems more important. For example, it is expected that body function will be maintained and improved if the person engages in mandatory high-intensity social activities. In contrast, the preference of the person for low-intensity and sedentary social activities cannot be expected to maintain and improve body function. The contents and characteristics of social activities that accompany social participation may have health implications.

Factors Related with Social Participation

Since social participation is a generic and broad concept, it is related to various factors. In the ICF, social participation is a component of living functions related to mental and physical functions, physical structure, activity, health conditions, individual factors, and environmental factors[3]. Previous reviews have reported that social participation is associated with cognitive and mental functions,

Table 1. Proposed taxonomy of social activities based on levels of involvement of the individual with others, and goals of these activities in older adults (Levasseur M, et al. 2010)[7]

Levels	Description of the levels of involvement	Individual proximity of involvement with others	Goals of the activity	Activities for whom or with whom	Examples using parental roles in relation to involvement in society
First level	Doing an activity in preparation for connecting with others	alone	basic needs oriented	for oneself	•The first level involves all daily activities that an individual normally does alone in preparation for other activities that will connect him/her with others. •These activities are basic and survival activities such as eating and dressing or can be more complex activities such as preparing meals (includes both activities of daily living and instrumental activities of daily living). •The person usually does the first level activities alone and in his/her home. •Example: solitary activities such as listening to the radio and watching TV, which informs himself/herself about what is going on in society.
Second level	Being with others (alone but with people around)	in parallel	basic needs oriented	for oneself	•The second level also includes activities where the individual is not directly in contact with others but others are around. •Example: the activities taken place in the community such as buy tickets online (Internet) and go alone to the cinema, execute financial transactions or shop for groceries without the services of a cashier, etc.
Third level	Interacting with others (social contact) without doing a specific activity with them	in interaction	socially oriented	(with others)	•In the third level, the individual is in social contact with others, in person or through the Internet, but does not do a specific activity with them. •Example: when shopping, the individual interacts with others to find what he/she wants or to pay for merchandise.
Fourth level	Doing an activity with others (collaborating to reach the same goal)	in interaction	task oriented	with others	•In the fourth level, the individual collaborates with others to perform an activity, reach a common goal. •Example: most recreational activities like tennis or shuffleboard. •Level three and four social activities include but are not restricted to social roles at a specific time or someone's personal situation (e.g. being a parent).
Fifth level	Helping others	in interaction	oriented toward helping others	with others	•The fifth level includes activities where the individual helps others. •Example: being a caregiver or volunteer. •A person or group of persons being helped can be identified.
Sixth level	Contributing to society	in interaction	society oriented	for others	•In the sixth level, the individual contributes more broadly to society (civic activities). •Example: being involved in political parties and organizations. •Contrary to the previous level, these contributions are seldom made solely by one individual and can potentially be beneficial to many persons, i.e. not intend to help specifically one person or a group of persons at the time, and interaction occurs with the community or society.

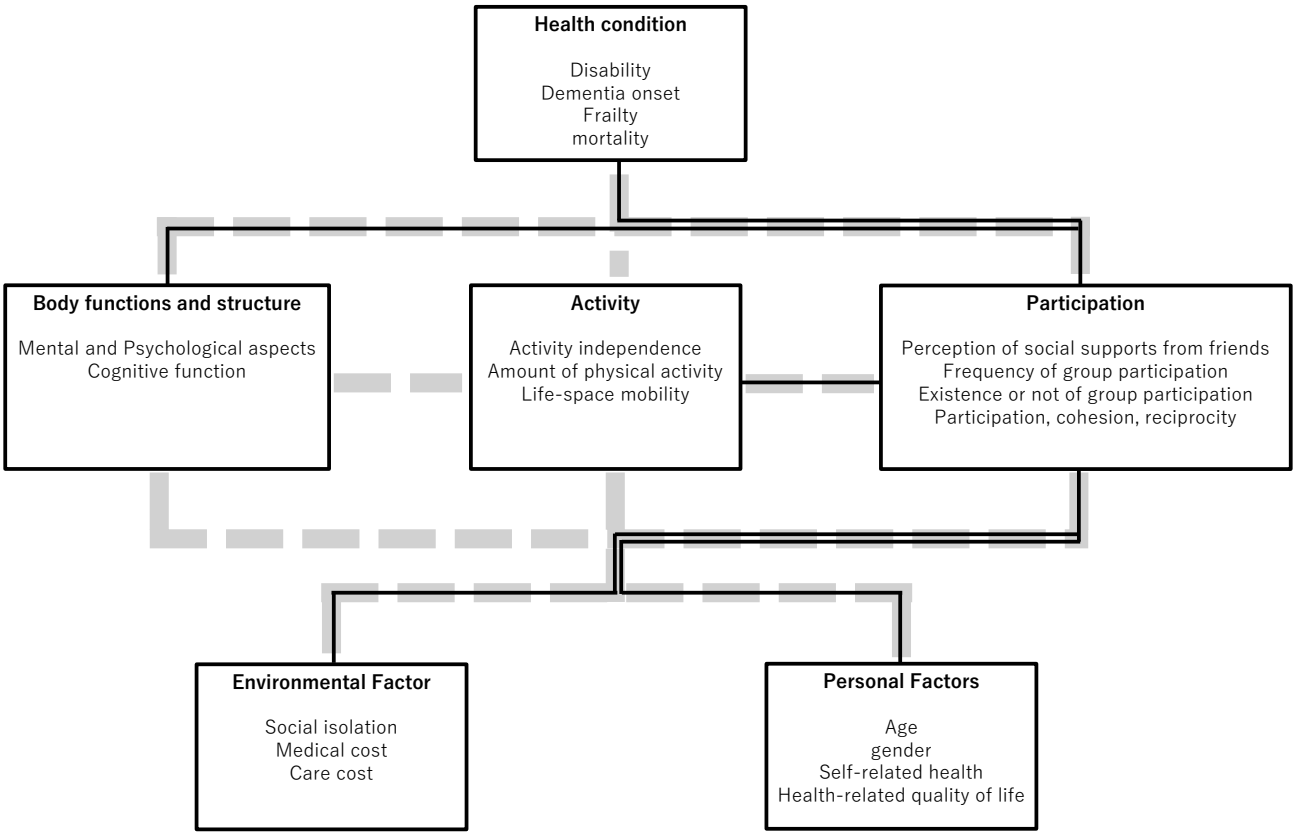

Fig. 1. A diagram based on ICF model as one representation of findings in previous studies that reported the related factors with social participation in Japanese older adults
Dashed line: Relationship between factors in the original ICF model
Solid line: Relationship with social participation reported in Japanese older adults

functional status, health-related adverse event in health condition, and health-related quality of life[12,15]. Although the factors related to social participation defined by each researcher have been investigated in each country, an international consensus on the definition of social participation has not been reached[2,7,8,12]. Additionally, the concepts of social participation and its restriction may differ across cultures[16,17] and neighborhood environments[18]. The factors related to social participation may also need to be investigated in detail according to the country or across countries. In the last 20 years, reports on social participation in older people have annually increased[1,2]. Most reports in terms of social participation in older people have been published in the United States, followed by Japan[2]. In Japan, the relationship between social participation and each factor in older adults has been investigated. In addition, in previous studies, social participation was associated with better cognitive function[19-23]; less depressive symptoms[24-28] and psychological distress[29]; more instrumental activities of daily living[30-32]; less functional disability[33-38]; better physical activity[39-41]; better life-space mobility[42]; better mental health[43]; self-related health[44] and health-related quality of life[45]; social isolation[46,47]; medical care costs[46,47]; and a lower incidence of dementia[48], frailty[49-51], and mortality[52] in Japanese older adults (Fig. 1). The factors associated with social participation in Japanese older adults are consistently similar to those reported in previous reviews[12,15].

When focusing on social activity, which is a component of social participation, activities involving older people positively or negatively correlate with demographic, biological, psychological, and cognitive factors; behavioral attitudes and skills; social and cultural factors; and environmental factors[53]. The participation of older adults in physical activity is a consequence that maintains and improves physical, cognitive, and psychological aspects and benefits health-related outcomes[54]. However, a disagreement exists as to whether exercise-based physical activity enhances social participation[55,56]. In other words, social participation with physical activity brings about a health benefit (physical function, structure, and activity in the ICF component) specific to the activity content; however, physical activity or enhanced physical function does not always enhance social participation. Complex interventions specific to the characteristics of various social participations (e.g., health status of the participating person, tasks to be carried out in the participation, and environment in which the participation is carried out) are required to obtain the benefits of enhancing social participation.

Assessment for Social Participation

Since there is no single instrument that can assess all aspects of health, no single instrument may be able to represent all aspects of social participation. There is no agreement regarding a standardized assessment and definition of social participation. There are different social participation characteristics depending on age, and social participation assessments linked to ICF[57-60] or the ICF-extended version for children and youth[61] have been proposed. Most instruments have been developed for adults including older adults with or without various diseases[57-60], and assess social participation only to a limited extent[62]. Family assessments of participation focus on the degree to which a person takes part in household, community, and society activities; fulfills roles; has relationships; and displays community presence. Social participation can be assessed as the performance expressed in various aspects[3,6,57], such as difficulty (restriction, limitation, and problem), independence, frequency, and hour[7]. The most common aspects of assessment for social participation include existence (participated or not); the degree of limitation, restriction, or difficulty; the degree of independence or need for assistance; and a count of the frequency or hours with which actions are performed in each type of social participation. Previous studies have identified social participation assessments that have acceptable levels of evidence of face, content, construct validity, and reliability to support their application to measure social participation[12,17,57-59] (Table 2). The instruments score the performance in social participation linking the ICF chapter domains of activity/participation[17,57-60], such as the presence/absence and degree of difficulty, frequency, importance, satisfaction, etc., and indicate the degree of social participation depending on whether the score is high or low.

Whether an individual participates or not may be determined by the following: 1) the feasibility to perform the participation, which is explained by the health condition of the individual and the environment surrounding the individual; 2) demand or duty for the individual to perform the participation based on a requirement from society or community; and 3) the importance and satisfaction to perform the participation determined by individual comprehension, appreciation, morality, obligation, and preference. Therefore, depending on the purpose of assessment for social participation, not only objectively assessing the performance of participation but also investigating subjective aspects, such as personal importance and satisfaction of social participation, are desirable (Fig. 2). Both objective and subjective measures of participation have been recommended as separate measures or even as separate subscales in a single instrument[6].

The ICF Measure of Activity and Participation Screener (IMPACT-S)[63]

The IMPACT-S is a self-report instrument for use in epidemiologic research assessing activity limitations and participation restrictions. It is composed of 32 items in 9 domains, each representing 1 of the 9 ICF activities and participation chapters. In this instrument, the ICF chapters 1-5 are designated as activities, and chapters 6-9 are designated as participation. The 32 items are scored by a three-point scale (0, cannot do that at all; 1, major limitations; 2, minor limitations; 3, no limitations whatsoever). Nine scale scores (1 per ICF domain), two subtotal scores for activities and participation, and a total score can be computed. All summary scores are averaged item scores and are converted to a 0-100 scale, with a high score indicating a high level of participation. The IMPACT-S covers the nine ICF domains of activities and participation.

Impact on Participation and Autonomy (IPA)[64,65]

The IPA is a self-report instrument focused on person-perceived participation and autonomy for use in a wide range of populations. The original instrument consisted of 23 items in 4 domains (social relationships, autonomy in self-care, mobility and leisure, and family role)[64]. The updated versions have 5 domains (autonomy indoors, family role, autonomy outdoors, social relations, and paid work and education) and 31 plus 8 additional items to address problem experiences[65]. The 31 items for perceived participation are scored by a five-point scale (1, very good; 2, good; 3, fair; 4, poor; 5, very poor). The eight items for perceived problems are scored with a three-point scale (0, no problems; 1, minor problem; 2, severe problem). For each domain, the participation and problem-experience scores are calculated by summing the item scores. The IPA score indicates chance of participation, and a high score shows more restrictions in participation and/or higher problem experience. The IPA covers the six ICF domains of mobility; self-care; domestic life; interpersonal relationships; major life areas; and community, social, and civic life.

Keele Assessment of Participation (KAP)[66]

The KAP is a self-report short instrument of 11 items for use in population surveys assessing the existence and degree of person-perceived participation restrictions. The 11 items are scored by a five-point scale (all the time, most of the time, some of the time, a little of the time, none of the time). Each item is dichotomized to define the presence (some, a little, or none of the time) or absence (all or most of the time) of participation restriction. Total scores are calculated by summing the number of items where restriction occurs (possible score of 0-11). The KAP covers the six

Table 2-1. Characteristics of the familiar instruments for social participation

Instrument	Aspects of participation performance	Total Items	Respondent burden	Linking of ICF chapter domain*									Examples of question items for the ICF domain of interpersonal relationships	Response options
				1	2	3	4	5	6	7	8	9		
IMPACT-S	Degree of limitation	32	not reported	✓	✓	✓	✓	✓	✓	✓	✓	✓	•Ask about the existence and degree of experienced limitations on social relations. E.g. general interpersonal interactions	0, cannot do that at all; 1, major limitations; 2, minor limitations; 3, no limitations whatsoever
IPA	Degree of goodness or severity for problem	39	20-minute				✓	✓	✓	✓	✓	✓	•Goodness 'The quality of my relationship with people who are close to me is ...' •Problem 'With regard to your relationships, to what extent does your health or disability cause problems?'	Goodness 1, very good; 2, good; 3, fair; 4, poor; 5, very poor Problem 0, no problems; 1, minor problem; 2, severe problem
KAP	Degree of limitation	11	3 minutes				✓	✓	✓	✓	✓	✓	•Ask about the existence and degree of restrictions on social relations. 'During the past 4 weeks, I have met and spoken to other people as and when I have wanted.'	0, no restriction (all or most of the time); 1, any restriction (some, a little, or none of the time)
P-Scale	Degree of limitation	18	20 minutes	✓		✓	✓	✓	✓	✓	✓	✓	'Are you comfortable meeting new people? [If sometimes, no or irrelevant] How big a problem is it to you?'	0, no restriction; 1, some restriction, but no problem; 2, small problem; 3, medium problem; 5, large problem
PAR-PRO	Degree of frequency	20	not reported				✓		✓	✓	✓	✓	Ask about frequency of home and community participation in any situations. E.g. Intimate relationship with a significant other	0, did not participate in this life situation; 1, participated monthly, once every 3–4 weeks; 2, participated bi-weekly, once every 2 weeks; 3, participated weekly, 1–4 days per week; 4, participated daily/almost daily, five or more days per week
PARTS/M	Degree of frequency, satisfaction, importance, and independence	135	60-90 minutes (paper-based) 25-40 minutes (web-based)				✓	✓	✓	✓	✓	✓	1. In a week, how frequently do you have intimate relations with another person? 2. Is your participation in intimacy limited by ... 3. How important is it for you to participate in intimacy? 4. To participate in intimacy, how much choice do you have compared to others without mobility limitations? 5. How satisfied are you with your participation in intimacy? 6. How much help from another person do you need to participate in intimacy? 7. How often do you use accommodations, adaptations or special equipment to participate in intimacy?	1. More than four times; 1-4 times; Less than once; Never 2. Illness; A physical impairment; Pain; Fatigue; Not limited 3. Very important; Somewhat important; Somewhat unimportant; Not important 4. A lot of choice; Some choice; Little choice; No choice 5. Very satisfied; Satisfied; Somewhat satisfied; Dissatisfied 6. A great deal; A moderate amount; Just a little; None 7. All of the time; Most of the time; Some of the time; A little of the time; Never
PM-PAC	Degree of limitation	51	45-60 minutes			✓	✓	✓	✓	✓	✓	✓	During the past week, how many friends or family members have you been in touch with (including those in your home) ?	None, one, two to four, five to eight, nine or more

*The ICF chapter domain: 1, learning and applying knowledge; 2, general tasks and demands; 3, communication; 4, mobility; 5, self-care; 6, domestic life; 7, interpersonal relationships; 8, major life areas; 9, community, social, and civic life.

IMPACT-S: ICF Measure of Activity and Participation Screener, IPA: Impact on Participation and Autonomy, KAP: Keele Assessment of Participation, P-scale: Participation scale, PAR-PRO: Participation Profile, PARTS/M: Participation Survey/Mobility, PM-PAC: Participation Measure for Post-Acute Care, POPS: Participation Objective Participation Subjective, ROPP: Rating of Perceived Participation, CHART: Craig Handicap Assessment and Reporting Technique, CIQ: Community Integration Questionnaire, WHODAS II: World Health Organization Disability Assessment Schedule II

Table 2-2. Characteristics of the familiar instruments for social participation

Instrument	Aspects of participation measurement	Total Items	Respondent burden	Linking of ICF chapter domain*									Examples of question items linking of the ICF domain of interpersonal relationships	Response options for the examples of question items
				1	2	3	4	5	6	7	8	9		
POPS	Degree of frequency, satisfaction, and importance	26	not reported			✓	✓		✓	✓	✓	✓	•Objective participation How many times in a typical week/month do you socialize with relatives, by phone or at home ? •Subjective participation (satisfaction) Would you say the amount you engage in socialize with relatives, by phone or at home is satisfactory for you? •Subjective participation (Importance) How important is socialize with relatives, by phone or at home to your satisfaction with life?	•Objective participation Frequency of occurrence of the activity in a week •Subjective participation (satisfaction) 3, same; 2, less; or 1, more •Subjective participation (Importance) 4, most; 3, very; 2, moderate; 1, little; or not important
ROPP	Degree of limitation, satisfaction, and want to support	22	15–30 minutes			✓	✓	✓	✓	✓	✓	✓	•Ask about level of perceived participation in social relationships. 'FULL PARTICIPATION is when one has an intimate relationship in the way and when one wants.' •Ask about satisfaction with the level of participation and want to support from the rehabilitation team to change the level of participation	•Level of participation 0, not restricted, not applicable; 1, mildly restricted; 2, moderately restricted; 3, very restricted; 4, severely restricted •Satisfaction with the level of participation •Want to support from the rehabilitation team to change the level of participation Yes or no
CHART	Degree of handicap	32	15 minutes				✓		✓	✓	✓	✓	How many relatives (not in your household) do you visit, phone, or write to at least once a month?	Add the number of children in household and number of other relatives in household to number of relatives contacted monthly. Multiply by 5. A maximum score for this component is 25 points.
CIQ	Degree of handicap	15	15 minutes				✓		✓	✓	✓	✓	Approximately how many times a month do you usually visit your friends and relatives?	0, seldom/never; 1, 1-4 times; 2, 5 or more
WHODAS II	Degree of difficulty	36	20 minutes	✓		✓	✓	✓	✓	✓	✓	✓	In the past 30 days, how much of a problem did your family have because of your health problems?	1, no difficulty; 2, mild difficulty; 3, moderate difficulty; 4, severe difficulty; and 5, extreme difficulty or cannot do

*The ICF chapter domain: 1, learning and applying knowledge; 2, general tasks and demands; 3, communication; 4, mobility; 5, self-care; 6, domestic life; 7, interpersonal relationships; 8, major life areas; 9, community, social, and civic life.

IMPACT-S: ICF Measure of Activity and Participation Screener, IPA: Impact on Participation and Autonomy, KAP: Keele Assessment of Participation, P-scale: Participation scale, PAR-PRO: Participation Profile, PARTS/M: Participation Survey/Mobility, PM-PAC: Participation Measure for Post-Acute Care, POPS: Participation Objective Participation Subjective, ROPP: Rating of Perceived Participation, CHART: Craig Handicap Assessment and Reporting Technique, CIQ: Community Integration Questionnaire, WHODAS II: World Health Organization Disability Assessment Schedule II

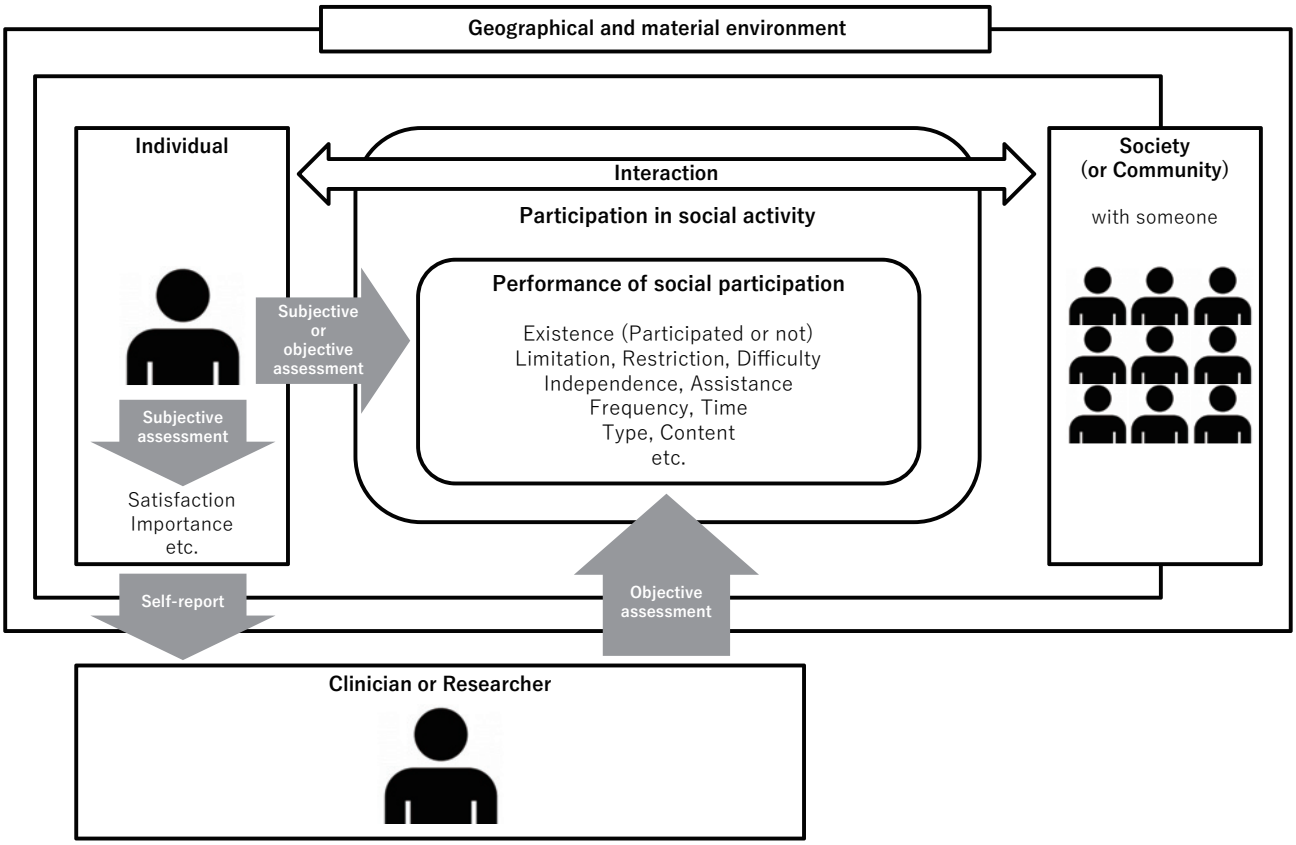

Fig. 2. A conceptual diagram of subjective and objective assessment for performance of social participation

ICF domains of mobility; self-care; domestic life; interpersonal relationships; major life areas; and community, social, and civic life.

Participation Scale (P-scale)[67]

The P-scale is an 18-item instrument assessing the severity of participation restrictions for people with leprosy, spinal cord injury, and polio or other conditions. The 18 items are scored by a five-point scale (0, no restriction; 1, some restriction, but no problem; 2, small problem; 3, medium problem; 5, large problem). Items are summed to obtain a total score ranging from 0 to 90. The P-scale score is interpreted as grades of participation restrictions with 0-12 indicating no significant restriction, 13-22 mild restriction, 23-32 moderate restriction, 33-52 severe restriction, and 53-90 extreme restriction. The P-scale covers the eight ICF domains of learning and applying knowledge; communication; mobility; self-care; domestic life; interpersonal relationships; major life areas; and community, social, and civic life, except for general tasks and demands.

Participation Profile (PAR-PRO)[68]

The PAR-PRO is a 20-item interview-based instrument assessing the frequency of home and community participation. The 20 items are scored with a five-point scale (0, did not participate in this life situation; 1, participated monthly, once every 3-4 weeks; 2, participated biweekly, once every 2 weeks; 3, participated weekly, 1-4 days per week; 4, participated daily/almost daily, five or more days per week). The original five-point score categories of 1 and 2 are combined into a category of 1 (activity occurred at least once a month but less than weekly), scoring categories of 3 and 4 combined into a category 2 (activity occurred at least once a week), and category 0 remained unchanged (activity did not occur) to yield a global participation score. Items are summed to obtain a total score ranging from 0 to 40. The PAR-PRO covers the five ICF domains of mobility; domestic life; interpersonal relationships; major life areas; and community, social, and civic life.

Participation Survey/Mobility (PARTS/M)[69]

The PARTS/M is a self-report instrument of 135 items assessing the generic participation of people with mobility impairments. The 135 items evaluate participation in 20 activities across the 6 ICF domains of mobility; self-care; domestic life; interpersonal relationships; major life areas; and community, social, and civic life. The scoring of each item is complex and based on principal component analysis results. Each of the 20 activities is evaluated by 6-8 questions based on frequency or time spent; importance, choice, and satisfaction; health-related limitations; and personal assis-

tance and environmental accommodations, adaptations, or special equipment. Finally, the instrument yields an overall score of participation, a participation score for each of the six domains, and four component scores (temporal: frequency and time taken; evaluative: choice, satisfaction, importance; health-related limitations; and supportive: human and environmental) for each domain. The PARTS/M provides a detailed description of participation based on multiple ratings. However, the assessment and scoring are long and complex.

Participation Measure for Post-Acute Care (PM-PAC)[70]

The PM-PAC is a self-report instrument of 51 items assessing participation in outpatient or home care settings. The 51 items evaluate participation across the seven ICF domains of communication; mobility; self-care; domestic life; interpersonal relationships; major life areas; and community, social, and civic life. The PM-PAC provides seven domain scores and two overall scores (social and home, and community). Higher scores indicate greater participation and satisfaction. However, no scoring algorithm is publicly available. The PM-PAC is complicated because it includes 12 different response options depending on each item.

Participation Objective, Participation Subjective (POPS)[71]

The POPS is an interview-based generic instrument assessing participation for any population. The instrument measures 26 activities across 5 domains of domestic life (8 activities); interpersonal relationships (8 activities); major life areas (3 activities); transportation (2 activities); and community, social, and civic life (5 activities). For each of the 26 activities, there are 3 questions, giving a total of 78 items. The first measures the frequency or duration of engagement (objective participation), the second measures how important engagement in the activity is, and the third refers to whether they would like to change their current level of engagement (subjective participation).

Scoring for the POPS is relatively complex and normalized using data from a sample of patients with traumatic brain injury and those with no disability. For objective participation, response options are measured as amounts: percentage of the activity that an individual is responsible for (domestic life domain); the number of hours per day, week, or month the activity is engaged in (major life areas domain); or the frequency of occurrence of the activity in a day, week, or month (all other domains). For scoring objective participation, all hour and frequency items are converted to a single base, frequency, or duration per month. Standardized scores are then calculated by subtracting the mean score for the item from each person's raw score for each item for the combined population norm and dividing by the standard deviation for the population. To control for outliers, standardized scores are set to −3 and +3. Standardized scores are then weighted by a factor that was the average of the mean importance rating of the population so that all items do not have equal weight (things that are done more have a greater weight). The score range for objective participation is −3 to 3, and the total score for objective participation is calculated as the average of the weighted standardized scores of the 26 items. Subscale scores can be calculated as the average standardized scores for the standardized samples. For subjective participation, the importance of each of the 26 activities to well-being is coded using the response options for how important (4, most; 3, very; 2, moderate; 1, little; or not important) and any change to current level of engagement (3, same; 2, less; or 1, more). For each of the 26 items, multiply the importance score by the satisfaction score, where a person who is wanting less or more is scored as −1 and his or her being satisfied with the current level is scored as +1. Scores can range from +4, indicating a most important area of life that the person is engaging in at a satisfactory level, to −4, indicating an equally important area of life that the person wants to do either less of or more. The score range for subjective participation is −4 to 4, and the subjective participation total score is the mean of the 26 activities. A computer is necessary to score this tool. Higher scores indicate greater participation.

Rating of Perceived Participation (ROPP)[72]

The ROPP is a self-report instrument assessing the level of perceived participation of a person. A total of 22 items evaluate participation across the 7 ICF domains of communication; mobility; self-care; domestic life; interpersonal relationships; major life areas; and community, social, and civic life. The 22 items of perceived participation are scored by a five-point scale (0, not restricted, not applicable; 1, mildly restricted; 2, moderately restricted; 3, very restricted; 4, severely restricted). Items are summed to obtain a total participation score ranging from 0 to 88. Questions about satisfaction with and desired support in changing the rated level of participation (yes/no) are additionally linked to each of the 22 items. An increasing score means increasing participation restriction.

Craig Handicap Assessment and Reporting Technique (CHART)[73,74]

The original CHART is an interview-based instrument of the degree to which impairments and disabilities result in handicaps based on five domains (physical independence, mobility, occupation, social integration, and economic self-sufficiency) of the International Classification of Impairments, Disabilities and Handicaps (ICIDH) framework[73].

The CHART items correspond well to the participation of the five ICF domains of mobility; domestic life; interpersonal relationships; major life areas; and community, social, and civic life[75]. Additional questions addressing the domain of cognitive independence were added to the CHART. The revised version contains 32 items of the ICIDH concept of handicap[74]. Scores on each subscale range from 0 to 100 with a total CHART score ranging from 0 to 600. Higher scores indicate a lower degree of handicaps or a greater degree of social participation.

Community Integration Questionnaire (CIQ)[76]

The CIQ is an instrument assessing handicap severity and participation restrictions for people with impairments and disabilities because of traumatic brain injury, chronic illness, or old age. A total of 15 items are divided into 3 domains of community integration: home integration (5 items), social integration (6 items), and productive activities (4 items). The scores report performance frequency, with additional weight given to whether or not assistance was obtained; 12 items are scored on a 3-point scale (0-2) and 3 items (productive employment, school, and volunteer activities) on a six-point scale (0-5). As a result of a summation of the scores from individual questions, the CIQ provides domain subscale and total scores ranging from 0 to 29. The CIQ items correspond to the participation of the five ICF domains of mobility; domestic life; interpersonal relationships; major life areas; and community, social, and civic life[77]. Three additional questions on integration into electronic social networking were added to the CIQ. The revised version of CIQ (CIQ-R) has a total of 18 items across 4 subscales: home integration, social integration, productivity, and participation in electronic social networking[78].

World Health Organization Disability Assessment Schedule II (WHODAS II)[79]

The WHODAS II is a generic self-report instrument to assess health and disability. Three versions of WHODAS 2.0 (36-item, 12-item, and 12 + 24-item version) were developed. The 36-item version consists of 36 Likert-format questions covering 6 domains: cognition, mobility, self-care, getting along, life activities, and participation in society during the previous 30 days. The assessed items of participation domain include social dimensions, such as community activities; barriers and hindrances in the world around the respondent; and problems with other issues, such as maintaining personal dignity. The items are answered in a five-point Likert scale (1, no difficulty; 2, mild difficulty; 3, moderate difficulty; 4, severe difficulty; 5, extreme difficulty or cannot do), grading the difficulty experienced by the respondent in performing a given activity. Each domain is separately weighted and scored. Domain-specific scores for six different domains and a total disability score can be calculated by converting them into a score ranging from 0 to 100. Higher scores indicate higher limitation/restriction in daily life.

Consideration in the Assessment of Social Participation

The usefulness of some instruments has not been fully examined as an assessment specific to older population[12] and are very complex in scoring. They do not specify the interpretation of the results and do not provide specific information[59]. Thus, explicitly stating how clearly these instruments can assess the social participation of older adults whose lifestyles differ from those of children and young adults is not possible.

Although activity and participation constructs are treated as one category with each distinctive definition in the ICF and the discussion on the distinction between the two has not been completed, both activity and participation can be demonstrated by the performance mentioned above. In terms of activity performance, the functional independence measure (FIM)[80] is a well-known assessment for activity centered on self-care; however, it only assesses activity limitation based on the degree of independence. To quantitatively assess the aspects of activity other than the degree of independence (e.g., amount and range of activity), conducting another assessment is necessary. This characteristic of the instrument is also common to social participation, and the participation restriction based on the degree of independence seems to be an outcome different from other quantitative aspects of social participation (e.g., frequency and time of social participation).

Additionally, basic activities of daily living that are common to each person and are carried out daily, and including the domains of activities for the assessment items that are also common to each person is possible. A gold standard, such as FIM[80], is applicable to assess the basic activities of many older people. In contrast, not everyone is doing all the social participation possible in this world. There is no agreement regarding which domains of social participation should be included in an assessment of participation. In a society, there may be social participation not only common to many older adults but also specialized to each older adult. Any variations in social participation can occur between individuals within a country (society) and between countries (societies), and the domains of "social participation that each person may carry out" and the "social participation that each person actually carries out" are different. Furthermore, what is normal social participation should be discussed with the definition of the concept of social participation, and there is concern that a certain social participation assessment can be defined as "normal social participation."

Conclusion

Because there are many factors related to diverse social participation and many limitations in the assessment of social participation, selecting the assessment of social participation according to what each clinician or researcher wants to investigate or developing a new assessment according to needs may be necessary. In future research, the common standardized concept and assessment is required, although using the definition, classification, and assessment of participation according to the purpose of research may be one of the important requirements.

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PHYSICAL
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REVIEW

Occupational Health Physiotherapy (OHP) Practice: A Comparison between Japan and Australia

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ABSTRACT. Objective: This study aimed to adapt a pre-existing cross-country comparison (CCC) model to Occupational Health Physiotherapy (OHP) practice as a basis for locating and examining contextual factors that may influence OHP practice in Japan and Australia. Method: A secondary analysis was conducted of existing publicly-available data on OHP and related influential factors, following the five components of the CCC model: work-related legislation; labor market characteristics; culture; physiotherapy practice norms; and organization of OHP practice. Results: Legislation in both countries promotes safe work and rehabilitation of work injured/ill workers. 2019 unemployment was lower in Japan with higher employment protection than Australia. Both countries have an ageing workforce and rising retirement age. Cultural differences relate to higher long-term orientation and uncertainty avoidance in Japan. Australia has higher individualism and physiotherapists are autonomous practitioners with direct access, which differs from Japan. Both countries have a national OHP subgroup, to date only Australia has OHP professional practice standards. Discussion: This study is the first to compare OHP practice in Japan and Australia. Contextual similarities and differences observed may underpin OHP practitioner role and its enhancement in work-related musculoskeletal disorder prevention and management strategies, the return-to-work process, and development of this physiotherapy discipline nationally. Conclusion: Adapting the CCC model to OHP practice enabled a structured exploration of resources and data, from which to extract and compare contextual factors that may shape OHP practice in Japan and Australia. This in turn may provide a useful springboard for further discussion about OHP practice internationally.

Key words: Occupational health and safety, Physiotherapy practice, Cross-country comparison model

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In the competitive world of employment, the health benefits of decent work have been widely endorsed[1)]. Work disability occurs when an employee's physical or mental health condition limits their ability to participate in paid employment[2,3)]. Within the employment domain, physiotherapists in the multidisciplinary healthcare team play an important role in reducing work disability[4)]. Physiotherapists are therefore well positioned to support their country's national economy by assisting employers in maintaining a

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healthy workforce, particularly in relation to work-related musculoskeletal disorders (WRMSDs)[5]. However, how physiotherapists operate in the field of occupational health and safety (OHS) may vary between countries, and investigating work-related physiotherapy practices may be the first step toward understanding similarities and differences in their role[6]. To date, there is no established "road map" of how best to make international comparisons of specific fields within occupational health physiotherapy (OHP)[7].

World Physiotherapy is the international body for physiotherapists; it has more than 120 member organizations and regularly conducts surveys to determine the "global state of the physiotherapy profession"[8]. World Physiotherapy divides their member organizations into five geographical regions[9]. The World Physiotherapy Asia Western Pacific region has member organisations in 30 countries including Japan and Australia[9] which are the focus of the current paper. Their World Physiotherapy member organizations are the Japanese Physical Therapy Association (JPTA) and the Australian Physiotherapy Association (APA)[8]. World Physiotherapy has formal subgroups for specific areas of practice that promote the advancement of physiotherapy and the exchange of scientific knowledge in their field[10]. The International Federation of Physical Therapists working in Occupational Health and Ergonomics (IFPTOHE) is a World Physiotherapy subgroup established in 2019[11]. Both the Japanese Society of Physical Therapy Section on Occupational Health (JSPTSOH) and Occupational Health Physiotherapy Australia (OHPA) are IFPTOHE member organisations[11]. Although these countries lie in the same World Physiotherapy region, they differ in both land mass and population size: while considerably smaller in size, Japan has a much larger population than Australia (approximately126 and 25 million people respectively)[12]. Both countries have an ageing population and consequently an ageing workforce[13]. High numbers of WRMSDs occur in both countries[14-17], with physiotherapists as stakeholders involved in their management. However, the similarities and differences in their work systems and customs related to OHP remain unexplored.

A cross-country comparison (CCC) model was developed by de Rijk[18,19] to enhance comparisons of factors influencing work disability prevention practices with the aim of learning about and from each other. In the same spirit, and with a view of strengthening knowledge about OHP practice, it seems appropriate to determine contextual influences that may underpin the similarities and differences of OHP practice in Japan and Australia. The objectives of the current paper were: to adapt the existing CCC model components to OHP; locate resources and data to satisfy the model's components; and to use them to describe/compare contextual factors in Japan and Australia that may influence OHP practice.

Methods

Study design

This study involved a secondary analysis of existing publicly-available data on OHP and related influential factors. As it did not involve human subjects, Human Research Ethics approval was not required. To direct the method of sourcing information, the authors used the framework of a cross-country comparison model (CCC model)[18,19] based on new institutional theory[20]. Although the model was designed for a different aspect of occupational health practice, it has recently provided a useful structure for the comparison of OHP practices between countries[6]. The model invites examination of five components: 1) Work-related legislation, 2) Labor market characteristics, 3) Culture, 4) Physiotherapy practice norms, and 5) Organization of OHP practice. Figure 1 shows the adaptation of the CCC model used for this study. Information retrieval was performed between March 2020 - April 2021.

Work-related Legislation

The authors defined "work-related legislation" as the formal societal rules and regulations of work and the workplace (for example, Acts) and the principles therein that relate to OHS and injury/illness management. We obtained the information related to this component of the model from the national work safety authorities' relevant web sites[21-23]. The authors also searched these websites for any guidelines about preventing and managing WRMSDs set by those authorities.

Labor market characteristics

Three labor market characteristics were compared: unemployment rate, employment protection level, and trend for retirement age. Unemployment rate reflects the underutilization of labour supply; we used the International Labour Organisation definition of unemployment which includes three criteria (not employed, looking, available)[24]. Employment protection level (2019) was examined in relation to the strictness of regulation about individual dismissals of regular workers, it provides an indication of job security with numbers ranging from 0-6, where the higher the figure the higher the social protection[25]. Information about national retirement age (2021 and future) was sourced from the Finnish Centre for Pensions[26].

Culture

Culture is defined as the collective ideas, customs, and behaviors of a certain group of people[27]. In his work on international business culture, Hofstede considered six dimensions: power distance, individualism, masculinity, uncertainty avoidance, long-term orientation, and indulgence. A brief definition of each of these terms is appended (Appendix 1). To determine the differences and similarities be-

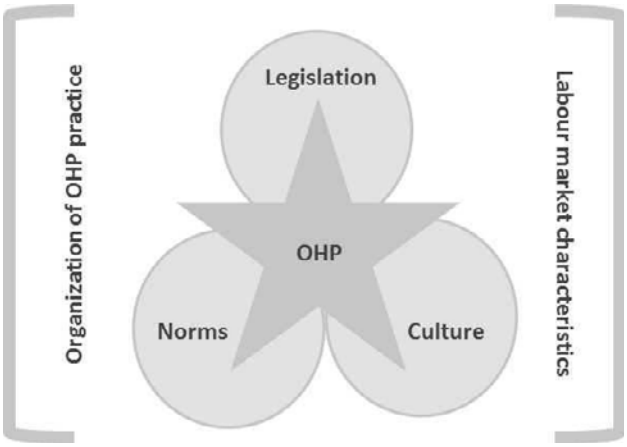

Fig. 1. Cross-country comparison model, adapted from Boucaut, et al. (2021), and based on the original model from de Rijk (2019), and de Rijk and Houkes (2019).

tween the Japanese and Australian cultures, we used the Hofstede's-insights comparison tool[27]. This scores different countries on each of the six dimensions using a numerical system (0-100), where a high score reflects a strong dimension. Prior physiotherapy researchers have also gained national perspectives using Hofstede's dimensions of culture[6,28,29].

Physiotherapy practice norms

The authors considered 'Norms' as the national conditions and parameters that guide physiotherapy professional practice. To determine these, we appraised several factors using data about national group profiles from the World Physiotherapy website (2020)[8]. This information included: demographics (number of physiotherapists in the national association group, practitioner/population ratio, and gender balance); minimum qualification required to practice (Degree or Diploma); nature of accreditation/registration; autonomy of practitioners and patient's direct access. We sought national guidelines related to WRMSDs prevention and management from medical and occupational health authorities and from the physiotherapy profession. Additionally we sought a description of the physiotherapy services currently provided to injured/ill workers including return to work services; seeking in Japan from the Ministry of Health Labour and Welfare website[14,15,30] and in Australia from a Regulator website in one jurisdiction, that being South Australia[31].

Organization of OHP practice

OHP practice involves "a range of measures aimed at reducing health and safety risks for people at work through injury *[and illness]* prevention and management"[32]. To determine the organization of OHP practice we compared the activities of the national OHP subgroups in each country: JSPTSOH and OHPA. Using World Physiotherapy, JPTA and APA websites, we gathered information on the date of subgroup formation in each country and where required contacted the national association directly (eg. for current subgroup membership data). We determined whether there were OHP professional practice standards[32,33] and whether there was guidance material to support practitioners about evidence based return to work practices. Finally, we sought to determine how physiotherapy students learn about OHP practice. To do this we compared the undergraduate curriculum (Bachelor degree program) at one university in each country, selected for convenience. These were the Kansai University of Welfare Sciences[34] and the University of South Australia[35] because the authors' affiliation with these institutions permitted access to internal program documents.

Findings

Work-related legislation

Both countries have legislation aimed at securing the safety and health of workers in workplaces and facilitating a positive work environment. In Japan, the Industrial Safety and Health Act[36] is the principal work legislation which together with the Labor Standards Act (Act No. 49 of 1947)[37] optimize national health and safety. In Australia there is similar legislation which is state based and nationally harmonized (eg South Australia has the Work Health and Safety Act, 2012)[38]. Australia also has state-based legislation regarding the management of injured/ill workers (including treatment); the over-arching aim is for Australian employers, where possible, to accommodate work injured/ill workers in terms of hours and duties and to facilitate a safe and durable return to work (eg South Australia has the Return to Work Act, 2014)[39]. In contrast, although the legislation in Japan contemplates the return to work of the injured worker and their consequent work accommodation by the employer, it leaves certain room for decision on the particular organization. There is guidance material from the Ministry of Health, Labour and Welfare in Japan to prevent work related LBP[40] and also prevention guidance from the Japan Industrial Safety and Health Association[41]. Safe Work Australia has practical guidance material to help employers prevent and manage WRMSDS more broadly[42].

Labor market characteristics

2019 unemployment figures were 2.4% in Japan and 5.2% in Australia[24]. OECD employment protection legislation indicators in 2019 were higher for Japan (2.1) than Australia (1.7)[25]. Both countries anticipate an increase of their retirement age: Japan from 63 to 65 (in 2025), and Australia from 66.6 to 67 (in 2023)[26].

Culture

The six cultural dimension scores from Hofstede's-

Table 1. Physiotherapy practice in Japan and Australia

Physiotherapy Practice Norms	Japan	Australia
National Association Members	104,610 (JPTA)	19,031 (APA)
Gender (%female)	36%	65%
Minimum qualification to practice	Diploma	Bachelors Degree
Is registration required to practice?	Yes (licence)	Yes
Scope of practice defined by	Ministry of Health or another government department (Government)	One or more independent regulation/ licensing/registration authorities (Independent)
Practice is guided by standards	Yes	Yes, more than one
Educated for autonomous practice?	No	Yes
Is direct access permitted?	No	Yes
Practising physiotherapists per 10,000 population	10.27	14.25
Telehealth services provision permitted	No	Yes

APA, Australian Physiotherapy Association; JPTA, Japanese Physical Therapy Association. Reference was 43.

insights tool for Japan and Australia respectively were: Power distance (54, 38); Individualism (46, 90); Masculinity (95, 61); Uncertainty avoidance (92, 51); Long term orientation (88, 21); Indulgence (42, 71)[27].

Physiotherapy practice norms

Information about physiotherapy practice demographics and norms in the two nations is presented in Table 1[43]. In Japan, the law dictates that all physiotherapy treatment interventions are directed by the medical profession, which influences how both physiotherapy practice and OHP practice are conducted[44]. In Japan in 2008, a medical fee for guidance on returning to work after an occupational injury was instated, which included physiotherapy services, under the workers' accident compensation insurance[45,46]. Only since 2013 have physiotherapists been allowed to conduct injury prevention initiatives at the workplace[47]. In South Australia, varied physiotherapy services may be conducted (with remuneration) in relation to work injury/illness, these include: Treatment in rooms, Workplace visit, Physiotherapy management plan, and Telehealth consultation[48]. Practice guidelines in Japan focus on the prevention of work-related LBP and are endorsed by national bodies external to the physiotherapy profession[41,49]. The Australian Physiotherapy Association is signatory to two guidelines relevant to the management of work injured/ill personnel. These relate to the health benefits of work[50] and evidence based clinical practice[51].

Organization of OHP practice

JSPTSOH was formed in 2013, and exceeded 6000 members in 2020[52]. OHPA was formed in the mid-1980s (previously termed the Ergonomics and Occupational Health group)[32]; as of March 2021 the group had 311 members, (personal communication with APA, 2021). OHPA has a pre-mapped career/training pathway for OHP practitioners and professional practice standards[53] for its members, JSPTSOH does not. The seven OHPA professional practice standards relate to: understanding work legislation, OHP knowledge, theoretically based interventions, tailored implementation, evaluation of efficacy, communication, and professional and ethical practice[53].

Discussion

General comments

To the best of our knowledge, this is the first investigation to compare Japan and Australia in relation to OHP practice. For this study, the authors refined the CCC model[6], that proved useful in the field of OHP practice, and was itself an adjustment of the original model from de Rijk[18,19]. In the pursuit of fulfilling the CCC model's requirements, the authors prioritized, where possible, the search of information in international resources/institutions that covered both countries, assuming they collect the data in an objective, homogeneous and independent manner.

Work-related legislation

Knowledge of work legislation is a requirement of OHP practice[53]. Laws in both Japan and Australia protect the safety and health of all workers providing potential opportunities for physiotherapists with their expertise in preventing and managing WRMSDs which is a leading occupational malady in both countries[14-17]. Work health and safety is achieved in both countries by promoting comprehensive and systematic measures for preventing industrial injuries/illnesses[17,36,37]. The Australian legislation encourages return to decent work where possible in line with current evidence[39]. Both countries have guidelines to prevent WRMSDs which could prove useful for OHP practitioners, and may reveal opportunities to learn from each other about OHP practice experiences. In Japan these include prevention measures for Low Back Pain at work[40], in Australia these encompass preventing WRMSDs more broadly using

a risk management approach[42]. Both countries share concerns about rising mental health issues in the community including at the workplace[54]. Knowledge of the interrelationship of mental health issues and WRMSDs is evolving, and may lead to a change in focus for all OHS stakeholders.

Labour market characteristics

Japan and Australia have differences in unemployment figures and Employment Protection. How these matters influence the role of the OHP practitioner warrants conjecture. Higher unemployment rates may encourage underreporting of non-fatal work injury such as WRMSDs[55]. Workers in countries with low employment protection could also be further disadvantaged in aspects of work accommodation and return-to-work in conditions of higher unemployment[56]. Physiotherapists including OHP practitioners may have reduced employment opportunities in times of high unemployment, which would likely change the ratio of physiotherapy practitioners (and possibly OHP practitioners) to head of population. The countries each have an ageing workforce, with increasing life expectancy and rising retirement age[26]. WRMSDs account for a high proportion of compensation costs, particularly among older workers[57]. National OHP subgroups have a strategic opportunity to promote OHP practitioners in assisting both employers and older workers by promoting health and wellness, providing treatment, appropriate work duties and tailored interventions[5].

Culture

National culture may influence business practices[58]. As OHS is important within business practices and as physiotherapists are stakeholders in multidisciplinary occupational health teams[5,59], we posit the potential impact of culture on OHP practice in the light of Hofstede's dimensions[27]. High long-term orientation in Japan may imply that once the field of OHP practice is embraced there, it could become a permanent component of business practice. Australian people tend to display more ease with uncertainty and seek as few rules as possible[27]. Australia implemented Robens-style OHS legislation in the mid 1980s with a self-regulating approach[60] in which stakeholders have broad duties. For Japan, reflecting on uncertainty avoidance could enable review of their current system and consideration of change strategies, such as expanding physiotherapists' work circumstances and environments to encompass OHP practice.

Both countries show competitive (masculine) traits. For OHP practice, competition related to productivity may possibly (negatively) influence the accommodation of injured workers concerning modified hours or duties, and employers/workers driven by competition might underreport WRMSDs. OHP practitioners in their quest to promote early and durable return-to-work need to weigh up the inherent benefits of work against possible re-injury. Worksite visits may facilitate OHP practitioners understanding of suitable work duties and accommodation[5,31].

Occupational health physiotherapists require sound communication skills[53] and egalitarian cultures may enable them to have useful discussions about suitable work duties with employees and supervisors at the workplace, and with Doctors about return-to-work. Low indulgence in Japan suggests that when OHP practitioners encourage accommodation and work hardening practices for return-to-work after injury/illness their efforts may result in some success and be durable. Individualism is higher in Australia than Japan. Perhaps this is reflected by autonomous physiotherapy practice in Australia, where being direct contact practitioners differs from Japan[43]. Legislative permission for this to change is an ongoing and future challenge for the Japanese physiotherapy profession.

Physiotherapy practice norms

Like the national population, the physiotherapy association size, and the OHP group size are all larger in Japan than in Australia, although the ratio of practising physiotherapists per 10,000 population is higher in Australia[43]. In terms of gender, physiotherapists in Japan are predominantly male, with the national gender employment gap remaining large and general work participation for women being limited[61]. In Australia, by contrast physiotherapists are predominantly female[43]. The influence on OHP practice derived from these gender differences among the workforce, national physiotherapists and OHP practitioners is yet to be determined.

The APA is signatory to both guidelines on the benefits of (decent) work[50] and clinical practice[51] providing Australian physiotherapists with clear direction for their interventions. Partnering with other stakeholders such as the medical profession clarifies that both professional groups support these initiatives. Having the JPTA or JSPTSOH as signatory on future medical guidelines may prove advantageous for both physiotherapy and OHP practice by highlighting an evidence based practice approach for practitioners, and alerting other stakeholders to the physiotherapeutic contribution in this field.

Besides on-site physiotherapy treatment in Australia, organisations in both countries may employ physiotherapists to conduct prevention and training at the workplace. In Japan work rehabilitation is only conducted in a medical setting[44,45]. The fee schedule for Return to Work SA (2020)[31] provides both clarity about what services physiotherapists currently provide for injured/ill workers in South Australia and the set fees. This accepted 'norm' for South Australian physiotherapists may be useful to frame future discussion about injury management practices in the two countries. The extended role of physiotherapists in the

authorization of work capacity certification for injured workers is a worthy future ambition[62,63]. Not without challenges, significant headway has already occurred on this matter in one Australian jurisdiction, Victoria[62].

In both countries, education for a bachelor degree is of four years duration. In Japan final examinations are set nationally by the Ministry of Health, Labour and Welfare[43] at the end of their study program requiring standardized curricula content, whereas in Australia university examinations are conducted throughout the program with some latitude for curricular content whilst meeting national competencies. These differences between the two countries may yield disparities in outcomes in knowledge, skills and competencies of OHP practitioners, whilst they share the challenge of incorporating OHP within their curricular content.

Organisation of OHP practice

OHPA has a longer history than JSPTSOH with more time to gain experience and develop processes. Both organisations advocate for OHP. Australia[53] and the United Kingdom[64] each have OHP professional practice standards requiring OHP practitioners to have good knowledge of OHP practice. At an organizational level these standards inform the choice and provision of educational material for group members and additionally provide marketing potential both within and external to the profession. JSPTSOH might consider whether future development of their own OHP professional practice standards would prove worthwhile.

Undergraduate education arguably may influence graduate choice of practice specialty[65]. The current status of OHP within international undergraduate curricula is unknown and a topic for further research. At the Kansai University of Welfare Sciences, Osaka, Japan, OHP training is included in the physiotherapy undergraduate core curriculum[34], and is limited to basic information about the role of physiotherapists in this field. At the University of South Australia "all final year students complete a five week course", including an industry placement[35], providing exposure to the nature of OHP practice[66]. Occupational health physiotherapists in Japan might benefit from further expanding their OHP training, perhaps following a similar approach to that of the Australian Physiotherapy Association/ OHPA in their quest to nationally promote OHP practice.

Strengths, Limitations and Future Directions

Two strengths of this study are that it is the first to attempt to compare OHP practice in Japan and Australia, and that the modified CCC model facilitated the investigators to explore some of the complexities that may influence OHP work. Therefore, the current study forms a basis for future comparative investigations between other nations. Some limitations are that there was no "guidebook" to help the investigators choose how best to define the five components of the model and the boundaries thereof, or where to find relevant supporting information. However, we anticipate that the current paper has initiated this process for use in future investigations.

Conclusion

The original cross-country comparison model developed by de Rijk A was adapted for relevance to OHP practice. The resulting model provided a structured approach to locate and analyse resources and data to satisfy the model's components, permitting a comparison of contextual factors that may influence OHP practice in Japan and Australia. Underlying factors that may influence OHP practice in two countries lying within the same World Physiotherapy region are presented. Findings revealed some similarities (eg work-related legislation) and differences (eg OHP national subgroup maturity and activities) between OHP practices. Using the CCC model may enable occupational health physiotherapists internationally to have structured dialogue about their work and thus learn about and from each other. Ultimately, being informed practitioners and educators we anticipate will lay the foundations to pave the way for improvements in this discipline globally.

Conflict of Interest: The authors declare that there is no relevant conflicts of interest.

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Supplementary material (Appendix):
Appendix 1. Hofstede's six cultural dimensions and their definitions.

Appendix 1.

Characteristic	Definitions
Power distance	*"…the extent to which the less powerful members of institutions and organisations within a country expect and accept that power is distributed unequally".*
Individualism	*"…the degree of interdependence a society maintains among its members".*
Masculinity	*"… what motivates people, wanting to be the best (Masculine) or liking what you do (Feminine)".*
Uncertainty avoidance	*"The extent to which the members of a culture feel threatened by ambiguous or unknown situations and have created beliefs and institutions that try to avoid these…".*
Long term orientation	*"…how every society has to maintain some links with its own past while dealing with the challenges of the present and future".*
Indulgence	*"…the extent to which people try to control their desires and impulses…".*

https://www.hofstede-insights.com/ (Accessed, 20 April 2021).

PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Relationships between Gross Motor Abilities and Sensory Processing in Children Aged 18 to 36 Months

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ABSTRACT. OBJECTIVE: We investigated the relationship between gross motor abilities and sensory processing in typically developing children. METHOD: Participants included children aged 18 to 36 months (N = 48). All participants were full-term infants. We assessed gross motor abilities based on the Gross Motor Function Measure (GMFM), and sensory processing characteristics based on the Infant/Toddler Sensory Profile (ITSP). The gross motor ability index was calculated using GMFM score which was estimated from the age. Pearson's product moment correlation coefficients were used to examine the relationships between the gross motor ability indexes and ITSP section scores. RESULTS: Our findings showed that gross motor ability may be related to oral sensory processing. The children who were more responsive to oral sensory processing tended to exhibit gross motor abilities below the standard for that age. CONCLUSION: Gross motor abilities were related with sensory processing, especially oral sensory processing, in children aged 18 to 36 months.

Key words: gross motor abilities, sensory processing, full-term infants

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Sensory processing is a broad term used to describe response to single sensory stimuli (e.g., sound or light), processing mechanisms within a specific sensory system, and integration of multiple sensory processing systems[1)]. These processes form the basis of learning, cognition and behavior in children[2)]. Typically developing children aged 1 to 3 years tend to acquire more sensory stimuli than children aged > 3 years[3)]. As children acquire more sensory stimuli and information, they experience habitation and sensitization[3)]. Habitation and sensitization permit children to generate appropriate adaptive responses to stimuli in the environment[3)]. Children with developmental disabilities, such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD), differ in sensory responses from typically developing children[4)]. As the sensory processing characteristics of typically developing children are distributed on the bell curve, some of them have sensory processing characteristics similar to those of cohorts with developmental disabilities[5)]. Ahn et al.[2)] reported that 5% of kindergarten children have sensory processing disorders.

Correct sensory processing is important during motor development because motor development is largely dependent on experiences, particularly active trial-and-error experiences[6)]. Currently, there are two common theoretical frameworks on motor development, the dynamic systems theory (DST)[7-9)], and the neuronal group selection theory (NGST)[10)]. In these theoretical frameworks, it is thought that experiences and correct sensory processing are essential for motor development. Correct sensory processing enables an adaptive response, the development of postural control, coordinated movement, motor development, and arrangement of the awake-orientation status[11)]. Previous studies have reported that motor development and sensory processing are related in preterm infants[11,12)]. As mentioned above, the sensory processing characteristics are distributed on the bell curve among full-term children[5)]. However, only

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a few studies have investigated the relationship between motor development and sensory processing among full-term children who demonstrated typical developmental patterns. Children aged 18 to 36 months spread their movement space after gaining the ability to walk stable. In addition, sensory processing characteristics might exhibit differences among individuals. Therefore, the purpose of the current study was to investigate the relationship between gross motor abilities and sensory processing in children aged 18 to 36 months.

Methods

Participants

Children aged 18 to 36 months were recruited through leaflet announcements from four nursery schools. Participants were excluded if they were premature or low birthweight infants, or if they had been diagnosed with developmental disorders, such as developmental coordination disorder (DCD), ASD, ADHD, intellectual disorder (ID), cerebral palsy (CP), or neurological or psychiatric disorders.

Prior to the study, written informed consent was obtained from the adult parents of each participating child in a manner approved by the research ethics committee of the Tokyo Metropolitan University Arakawa Campus (approval number 19059).

Instruments

Two standardized measuring instruments were used in the current study. We assessed sensory processing characteristics based on the Infant / Toddler Sensory Profile (ITSP)[13], and gross motor abilities were assessed based on the Gross Motor Function Measure (GMFM)[14].

Japanese Version of ITSP (J-ITSP)[15]

The ITSP is a standardized parent-reported questionnaire that is used to assess sensory processing characteristics in infants and toddlers. There are two types of ITSP questionnaires: a) the first is for children aged 0 to 6 months, and b) the second is for children aged 7 to 36 months. In the current study, we used the ITSP for children aged 7 to 36 months according to the participants' age. In this case, the ITSP consisted of 48 items. Parents or caregivers rated the frequency of their child's sensory processing characteristics and behaviors based on a five-point Likert scale: 5 = always, 4 = frequently, 3 = occasionally, 2 = seldom, and 1 = never. Items were grouped in the following five sensory system sections: auditory processing (13 items), visual processing (7 items), tactile processing (15 items), vestibular processing (6 items), and oral sensory processing (7 items). Three items refer to general processing types. The scores for the five sections were calculated by summation of all the points for all the items in a section. The reliabilities of the J-ITSP for various composite scores ranged from .56-.90[15].

GMFM

The GMFM is a standardized observational instrument designed to measure gross motor abilities over time for children with CP aged 5 months to 16 years. Because the items included in the GMFM are typical for normal developmental milestones in 5 year old children, we used GMFM to measure gross motor abilities. There are two versions of GMFM: a) the first one is the original measure with 88 items (GMFM-88) and b) the second is a measure with 66 items (GMFM-66). The GMFM-88 has been validated in populations other than CP, such as Down syndrome[16,17], traumatic brain injury[18], Fukuyama congenital muscular dystrophy[19], and osteogenesis imperfecta[20]. The items are scored on a four-point ordinal scale: 0 = cannot initiate, 1 = initiates, 2 = partially completes item, 3 = completes item independently[14]. We adopted the GMFM-66 that was developed based on Rasch analysis in an attempt to improve the interpretability and clinical usefulness of the GMFM-88[21]. GMFM-66 has good reliability and validity (intraclass correlation [ICC] = .96)[22]. Furthermore, we adopted the 'basal-ceiling' approach of GMFM-66 (GMFM-66 B&C). During the administration of GMFM-66 B&C, testing began once three consecutive "3s" ("completes") had been scored, and stopped when three consecutive "0s" ("does not initiate") had been scored. To complete the test, at least 15 items should be tested[14]. GMFM-66 B&C has good reliability and validity with GMFM-66 (ICC = .99, 95% confidence interval = .98- .99)[23]. The individual item scores of GMFM-66 are converted to an interval score using a computer program called "GMFM App+"[14]. The GMFM-66 score (GMFM score) ranges from 0 to 100. The GMFM score of typically developing child aged 5 years is expected to be 100.

Prior to the study, we examined the test-retest reliability of GMFM-66 B&C with 11 children. Eleven children were randomly elected from the participants. One rater assessed the GMFM-66 B&C following a 2-3 week interval. As a result, ICC was excellent[24] (ICC (1, 2) = .97). There was a significant and strong correlation between the GMFM score and age in months ($r = .751$, $p < .01$). Therefore, we confirmed the reliability and validity in the assessment of GMFM in typically developing children, and it was possible to assess typically developing children based on the GMFM.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics (Version 22.0; IBM Corp., Armonk, NY). Descriptive statistics were used to characterize the basic properties of the observed variables. In order to remove the influence of age, the gross motor ability index was adopted. Single linear regression models were applied to calculate

Table 1. Mean Scores for J-ITSP Sensory Systems Sections

Sensory systems sections		Mean	SD
Auditory	(13 items)	16.1	5.0
Visual	(7 items)	14.4	5.1
Tactile	(15 items)	24.9	5.8
Vestibular	(6 items)	12.7	3.1
Oral sensory	(7 items)	11.3	4.3

Note. SD = standard deviation, J-ITSP = Japanese version of Infant/Toddler Sensory Profile.

Table 2. Rerationship between J-ITSP Section Scores and Age in Months

Sensory systems sections		Age in Months	
		r	p
Auditory	(13 items)	-0.159	0.280
Visual	(7 items)	0.128	0.385
Tactile	(15 items)	-0.166	0.261
Vestibular	(6 items)	0.185	0.208
Oral sensory	(7 items)	-0.140	0.343

Note. J-ITSP = Japanese version of Infant/Toddler Sensory Profile, r = Pearson's product moment correlation coefficirnts.

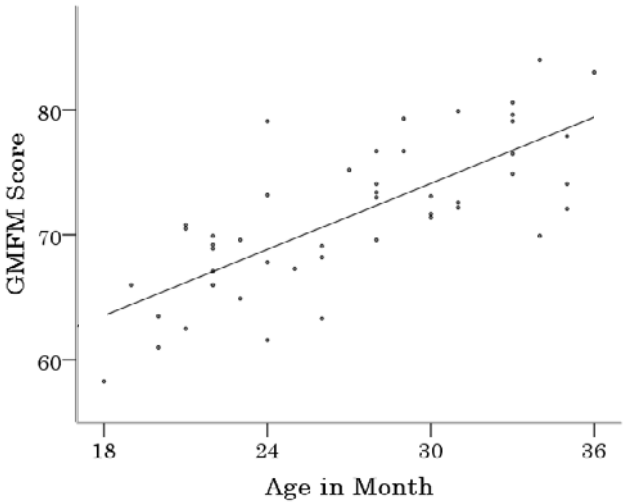

Figure 1. Scatter plot and linear regression analysis conducted to investigate the association between the GMFM score and age in months.
Note. GMFM = Gross Motor Function Measure.

the standard GMFM scores estimated from the ages of participants. The independent variable was age in months, whereas the GMFM score was examined as the dependent variable in the regression analyses. The GMFM scores were calculated with the use of the estimated regression formula. The gross motor ability index was defined as the difference between the assessed and estimated GMFM scores. If the gross motor ability index is zero, the gross motor ability is standard for the age. A positive gross motor ability index is above the standard for the age, whereas a negative gross motor ability index is below the standard for the age. Pearson's product moment correlation coefficients were used to examine the relationships between age in months, gross motor abilities and sensory processing characteristics. Spearman's rank correlation coefficients were used to examine the relationships between gross motor abilities and ITSP item points. Correlation coefficients were interpreted as follows: strong correlation ($r > .75$), moderate correlation (r = .50-.75), mild correlation (r = .25-.50), and weak correlation ($r < .25$). Significance was set at $p < .05$.

Results

Demographic Characteristics of Participants

Forty-eight participants who demonstrated typical developmental patterns were enrolled in the current study. The participants' mean age was 27.1 months (standard deviation [SD] = 5.1, range 18-36 months), with 27 boys and 21 girls. The mean height was 85.2 cm (SD = 4.4, range 74.1-94.9 cm), mean weight was 12.0 kg (SD = 1.5, range 9.2-14.8 kg), mean gestational age was 39.2 weeks (SD = 1.1, Range 37-41 weeks), and the mean birth weight was 3164.1 g (SD = 389.7, range 2500-4300 g).

J-ITSP Score

The mean scores for the J-ITSP sensory system sections are displayed in Table 1. There were no significant relationships between the J-ITSP section scores and age in months (See Table 2).

GMFM Score

The participants' mean GMFM score was 71.6 (SD = 6.0, range 58-84). By conducting single linear regression with age in months as the independent variable and the GMFM score as the dependent variable, the following significant regression formula was obtained: GMFM score = 47.668 + 0.882 × age in months ($p < .01$, $r^2 = .564$, see Figure 1).

Relationship between the Gross Motor Ability Index and Sensory Processing

There was a significant relationship between the gross motor ability index and oral sensory processing ($p = .045$). There were no significant relationships between the gross motor ability index and the other J-ITSP section scores (See Table 3). Among the oral sensory processing items, item 42 ("My child licks / chews on nonfood objects."), was significantly associated with the gross motor ability index ($p = .030$, see Table 4). Figure 2 shows the distribution of item 42. The median is 1.0. The highest frequency is 31 (64.6%) for 1 within a five-point Likert scale. The distribution of

item 42 is the most common pattern. Twenty nine of 48 items (60.9%) showed similar distribution.

Discussion

We investigated the relationship between gross motor abilities and sensory processing in full-term children who demonstrated typical developmental patterns (aged 18 to 36 months). Our findings showed that gross motor ability may be related to oral sensory processing. Children who were more responsive to oral sensory processing tended to exhibit gross motor abilities below the usual standard for that age.

Oral sensory processing is important in children. In particular, the mouth is a major source of receiving information during the early developmental period[3]. The mouth and face are structures that occupy most of the area of the sensory homunculus, which shows the sensory distribution of the body in the cerebral cortex[25].

Furthermore item 42 ("My child licks / chews on nonfood objects.") related to sensory seeking[13] and exploratory behaviors. Exploratory behavior through oral sensory processing is also important during childhood development. In early development, sucking provides infants with essential nutrients, the feeling of well-being, and the sense of security[26]. As infants develop, they seek and explore through oral sensory processing based on mouthing behaviors, such as sucking their fingers and any objects that come in contact with their mouths. Oral sensory processing in combination with visual processing and tactile processing allows children to explore their environments[27,28].

The frequency of mouthing behavior in children may be affected by age[26,29,30]. Tulve et al.[31] reported that the frequency of mouthing behavior decreased in children aged ≤ 2 years. Conversely, Bearmer et al.[32] observed mouthing behaviors, such as those related to the placement of clothes and plastics to their mouths in children aged > 7 years. The frequency of exploratory behaviors through oral sensory processing decreases with age; however, this may vary

Table 3. Rerationship between Gross Motor Ability Index and J-ITSP Section Scores

Sensory systems sections	Gross Motor Ability Index	
	r	p
Auditory	-0.172	0.242
Visual	-0.284	0.051
Tactile	0.037	0.804
Vestibular	-0.049	0.742
Oral sensory	-0.291*	0.045

Note. Gross Motor Ability Index = the defference between assessed GMFM score and estimated GMFM score, GMFM = Gross Motor Function Measure, J-ITSP = Japanese version of Infant/Toddler Sensory Profile, r = Pearson's product moment correlation coefficirnts.

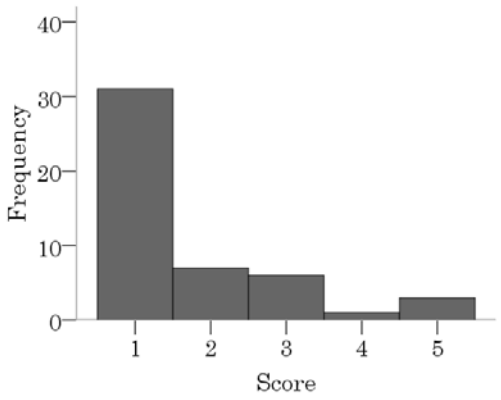

Figure 2. Histogram of J-ITSP Item 42.
Note. J-ITSP = Japanese version of Infant/Toddler Sensory Profile.

Table 4. Rerationship between Gross Motor Ability Index and J-ITSP Items in Oral Sensory Processing

J-ITSP Items in Oral Sensory Processing	Gross Motor Ability Index	
	r_s	p
42 My child licks / chews on nonfood objects.	-0.314*	0.030
43 My child mouths objects.	-0.269	0.064
44 My child does not notice food and drink remain on his / her lip.	0.164	0.264
45 My child eats a few kinds of foods.	0.031	0.832
46 My child resists having teeth brushed.	-0.243	0.096
47 My child resists to drink from a glass.	0.047	0.749
48 My child resists to try new kinds of food.	-0.009	0.952

Note. Gross Motor Ability Index = the defference between assessed GMFM score and estimated GMFM score, GMFM = Gross Motor Function Measure, J-ITSP = Japanese version of Infant/Toddler Sensory Profile, r_s = Spearman's rank correlation coefficients.

from child to child.

According to Piaget's theory of child cognitive development, the sensorimotor stage occurs from birth to 2 years[33]. Children aged ≤ 3 years may acquire more information[3]. As sensory and motor signals are inextricably linked[34], gross motor ability is related to oral sensory processing. Thus, oral sensory processing could be an indicator of gross motor abilities.

A limitation of the current study was that our sample size was small. This also limits the conclusions that were determined by the calculated gross motor ability index within our sample. Additionally, the regression formula obtained in the current study was calculated within our sample. Therefore, it cannot explain the relationships between age and gross motor ability in other age groups. To confirm our results, future studies with larger sample sizes and higher variance among participants are needed.

Conclusion

The current study revealed that gross motor abilities are related to sensory processing, especially oral sensory processing. Full-term children aged 18 to 36 months with responsiveness in oral sensory processing tended to exhibit gross motor abilities below the standard for that age.

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Conflict of Interest: The authors disclose no conflicts of interest.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Effect of a Combined Exercise and Cognitive Activity Intervention on Cognitive Function in Community-dwelling Older Adults: A Pilot Randomized Controlled Trial

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ABSTRACT. Objective: The purpose of this study is to investigate the effect of an intervention combining exercise and cognitive activity on cognitive function in healthy older adults. Methods: This pilot randomized controlled trial recruited 33 eligible, healthy communitydwelling older adults (mean age, 77.1 years old; women, 51.5%), who were divided into intervention and waitlist control groups. The intervention group was engaged weekly in a group activity comprising exercise and discussions of homework, which included reading aloud, simple arithmetic, and simple activities, like spotting differences, for cognitive stimulation. They were also required to complete cognitive activity homework twice a week. The waitlist control group received no intervention. The main outcomes were cognitive function assessed using the Mini-Mental State Examination, delayed recall score on the Logical Memory IIA of the Wechsler Memory Scale Revised, Trail Making Test, and digit symbol substitution test. Results: According to the results, Mini-Mental State Examination scores were maintained in the intervention group but declined in the control group [Mean change in outcomes in control group (95% confidence interval): -1.68 (-2.89 to -0.48)]. Additional mean change in outcomes in intervention group were found [1.68 (0.02 to 3.35)]. Conclusions: Interventions combining exercise and cognitive activity can be helpful for preserving cognitive function in healthy older adults.

Key words: Cognitive activity, Cognitive functon, Exercise, Older adults

(Phys Ther Res 24: 112-119, 2021)

The prevalence of Alzheimer's disease has significantly increased with the expansion of the older adult population, and as per estimates, the current 33.9 million cases worldwide will triple by 2050[1,2]. In particular, the already high prevalence of dementia in Asian countries will only increase further[2]. Further, the incidence of dementia has been reported to be decreasing in Western countries over time; meanwhile, it has been increasing in Japan[3-5]. This implies that the prevention of dementia is essential in Japan. Prevention of dementia is still a critical unmet medical need, and many researches failed to develop disease-modifying therapies for Alzheimer's disease[6].

Exercise has received much attention as a possible preventive strategy for dementia. This is unsurprising, given its positive effects on cardiovascular health, diabetes, and mental health, which are reported to be modifiable risk factors for dementia[7]. Sufficient amounts of exercise are reported to be equivalent to polypills and have a low risk of adverse effects[8]. A meta-analysis published in 2019 revealed a small effect of exercise on cognitive function in healthy older adults including aerobic and resistance training (Hedge's g = 0.31); however, this study entailed a pub-

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lication bias[9]. Recently, it is pointed out that a combination of exercise and cognitive activity may be more efficacious for the improvement of cognitive function in healthy older adults. A meta-analysis including non-randomized control studies suggested that the combination training improves cognitive function more than physical exercise alone and control in healthy older adults[10]. However, there is a need for more randomized controlled trials investigating this combination effect, especially in Asian countries, where there have so far been only two studies of this type in healthy older adults[11,12].

The purpose of this study is to investigate the effect of an intervention combining exercise and cognitive activity on cognitive function in community-dwelling older adults.

Methods

Design, setting, and participants

This randomized controlled trial was conducted between June 2017 and March 2018. Community-dwelling older adults were recruited from Tomogaoka, Northern Suma area, in Kobe city. Posters describing the study were displayed at community centers and invitation letters were sent to recruit participants. Thirty-four older adults agreed to participate in this trial. The inclusion criteria were older adults who: 1) were aged 70 years or above and 2) could walk independently 3) had no cognitive decline (Mini-Mental State Examination (MMSE) score > 24). The exclusion criteria were chronic diseases that hindered physical activity. After excluding one respondent owing to cognitive decline, 33 participants were included in the study (mean age, 77.1 years old; women, 51.5%). Respondents received no incentive, monetary or otherwise, for participation in this trial. They were divided into two groups: intervention group (n=17) and wait-list control (n=16). Baseline assessment except for cognitive function was conducted on June 6 and 7, 2017, and baseline cognitive assessment was conducted between June 8 and 14. The intervention duration was from June 28 to September 20. Immediate follow-up assessment except for cognitive function was conducted on September 21 and 22, and follow-up cognitive function assessment was conducted between September 25 and 29. Additional follow-up assessment was conducted between February 26 and March 23, 2018, which was determined randomly. No intervention was conducted on the intervention group between immediate follow-up (September 2017) and additional refollow-up (February and March 2018).

The Research Ethics Committee of Kobe University Graduate School of Health Sciences approved the study (authorization number 592), and written informed consent was obtained from all participants. This randomized controlled trial was conducted in accordance with CONSORT criteria (Table S1) (registration number: UMIN000027740; https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000031784).

Intervention group

The intervention comprised two components: group activity and homework. Every group activity was conducted after a physical and vitals check.

Group activity, which included exercise and discussing homework, was conducted once weekly for three months. During the abovementioned intervention period, we skipped one week because of a traditional Japanese holiday. In total, group activity was conducted 12 times. Trained physiotherapists supervised this program. Each class contained 5-15 participants. The first group activity session included an orientation, where the supervisor provided an explanation of the importance of exercise and cognitive activity for preserving cognitive function. Here, participants were informed about the homework and physical activity requirements. In the second and third sessions, cognitive activity was conducted to teach how to do homework more detail after checking the answer of homework (35 min), stretching and muscle strength training (30 min), and dual-task aerobic exercise (20 min). Sessions 4 to 12, which were 90 minutes long, involved discussing homework (25 min), stretching and muscle strength training (30 min), and dual-task aerobic exercise (30 min). Participants were given a break every 30 minutes. In the dual-task aerobic exercise, participants performed physical activity (a step exercise using a platform) while making calculations, taking verbal fluency tests (categories and letters), or playing a Japanese word chain game called "Shiritori," wherein the person in question has to name a word beginning with the final letter of the previous word. The cognitive activity contents were based on previous studies[13,14]. The participants received two sets of homework after group activity: reading aloud and simple arithmetic[13]. Additionally, the homework sheets included tasks that involved spotting differences, searching task, and riddles[14]. A previous study used a computer-based cognitive activity tool, "Atama-no-dojo," and we used its paper-and-pencil version[14]. The supervisor asked the participants to do the homework twice a week and bring it to the following week's group activity.

Waitlist control group

The waitlist control group received no intervention in the trial period. After three months, this group received the identical intervention.

Randomization and blinding

Simple randomization was conducted. Participants were randomly divided into two groups with 1:1 allocation as per a computer-generated randomization schedule. The first author created two categories (0 or 1) based on random numbers. To ensure concealed allocation, the researcher conducting the randomization was blinded to which number

Table 1. Comparison of Baseline Demographic and Clinical Characteristics Between the Groups

	Control (n = 16)	Intervention (n = 17)	*p*
Age, years, mean (SD)	76.81 (3.60)	77.35 (3.94)	0.684
Women, n (%)	10 (62.5)	7 (41.2)	0.303
BMI, kg/m^2, mean (SD)	23.37 (2.06)	23.78 (3.95)	0.725
Missing, n (%)	1 (6.3)	0 (0.0)	
Systolic blood pressure, mmHg, mean (SD)	139.47 (11.27)	141.47 (23.18)	0.763
Missing, n (%)	1 (6.3)	0 (0.0)	
Diastolic blood pressure, mmHg, mean (SD)	80.13 (7.13)	81.71 (13.76)	0.694
Missing	1 (6.3)	0 (0.0)	
Smoking status, n (%)			0.141
Never smoker	12 (75.0)	9 (52.9)	
Ex-smoker	3 (18.8)	8 (47.1)	
Current smoker	1 (6.2)	0 (0.0)	
Alcohol consumption, n (%)			1
No	4 (25.0)	3 (17.6)	
Rarely	3 (18.8)	4 (23.5)	
Sometimes	2 (12.5)	3 (17.6)	
Every day	7 (43.8)	7 (41.2)	
Education, years, n (%)			0.534
< 10 years	3 (18.8)	4 (23.5)	
10-12 years	7 (43.8)	10 (58.8)	
> 12 years	6 (37.5)	3 (17.6)	
Household income, n (%)			0.518
< 2 million	3 (18.8)	4 (23.5)	
2-4 million	9 (56.2)	10 (58.8)	
4-6 million	1 (6.2)	3 (17.6)	
6-8 million	2 (12.5)	0 (0.0)	
≥ 8 million	0 (0.0)	0 (0.0)	
Missing	1 (6.2)	0 (0.0)	
Comorbidities			
Hypertension, n (%)	6 (37.5)	8 (47.1)	0.728
Stroke, n (%)	0 (0.0)	0 (0.0)	NA
Diabetes, n (%)	1 (6.2)	2 (11.8)	1
Parkinson's disease, n (%)	0 (0.0)	0 (0.0)	NA
Hyperlipidemia, n (%)	3 (18.8)	2 (11.8)	0.656
Knee osteoarthritis, n (%)	3 (18.8)	3 (17.6)	1
Cancer, n (%)	2 (12.5)	2 (11.8)	1
Respiratory illness, n (%)	0 (0.0)	2 (11.8)	0.485
Heart disease, n (%)	2 (12.5)	3 (17.6)	1
Medication type			
Tranquilizer, n (%)	0 (0.0)	0 (0.0)	1
Analgesic, n (%)	1 (6.2)	4 (23.5)	0.335
Depressor, n (%)	7 (43.8)	11 (64.7)	0.303
Antidepressant, n (%)	0 (0.0)	0 (0.0)	NA
Blood samples			
Total cholesterol, mg/dl, mean (SD)	219.62 (29.75)	198.24 (33.03)	0.06
HDL, mg/dl, mean (SD)	71.75 (20.81)	63.59 (18.23)	0.239
Triglyceride mg/dl, mean (SD)	168.50 (111.87)	131.06 (61.87)	0.239
Blood sugar mg/dl, mean (SD)	106.94 (32.91)	94.35 (10.41)	0.144
HbA1c, %, mean (SD)	5.81 (0.55)	5.73 (0.41)	0.622
Physical measurements			
Gait speed, s/m, mean (SD)	1.23 (0.19)	1.19 (0.19)	0.613
Grip strength, kg, mean (SD)	26.50 (9.64)	27.12 (6.06)	0.825

Table 1. Comparison of Baseline Demographic and Clinical Characteristics Between the Groups (continued)

	Control (n = 16)	Intervention (n = 17)	*p*
Timed Up-and-Go Test, sec, mean (SD)	8.97 (1.88)	8.99 (1.44)	0.969
Depressive symptoms, n (%)	0 (0.0)	4 (23.5)	0.103
Missing	1 (6.2)	0 (0.0)	
Cognitive assessments			
MMSE, point, mean (SD)	28.50 (1.67)	27.47 (1.91)	0.11
TMT-A, sec, mean (SD)	44.49 (11.72)	45.43 (9.75)	0.803
TMT-B, sec, mean (SD)	117.45 (46.52)	117.90 (59.41)	0.981
Missing	0 (0.0)	1 (5.9)	
DSST, count, mean (SD)	45.19 (10.37)	43.94 (10.76)	0.737
WMS-R short-term, count, mean (SD)	10.31 (4.56)	7.88 (3.87)	0.108
WMS-R long-term, count, mean (SD)	7.69 (4.05)	7.35 (4.29)	0.819

Abbreviations: SD, standard deviation; NA, not available; BMI, body mass index; HDL, high-density lipoprotein; HbA1c, hemoglobin A1c; MMSE, Mini-Mental State Examination; TMT, Trail Making Test; DSST, digit symbol substitution test; WMS-R, Logical Memory subtest of the Wechsler Memory Scale Revised

indicated the intervention group and which one indicated the waitlist control group. No other blinding, such as of subjects, therapists, and assessor, was conducted.

Outcome

Outcome was measured thrice in the intervention group—at baseline, follow-up three months after baseline assessment, and five months after the conclusion of the intervention— and twice in the waitlist control group—at baseline and follow-up.

Cognitive function was evaluated using the MMSE[15], delayed recall score on the Logical Memory IIA (LM IIA) of the Wechsler Memory Scale Revised, Trail Making Test[16], and digit symbol substitution test from the Wechsler Adult Intelligence Scale-Revised[17].

Other measurements

The other data, collected using a self-reported questionnaire, included age, sex, smoking status (never smoker, ex-smoker, current smoker), alcohol consumption (never, rarely, sometimes, every day), number of medications, medication type (tranquilizer, analgesic, depressor, antidepressant), education (< 10 years, 10-12 years, > 12 years), comorbidities (hypertension, stroke, diabetes, Parkinson's disease, hyperlipidemia, knee osteoarthritis, disc herniation, compression fracture, spinal canal stenosis, rheumatoid arthritis, cancer, respiratory illness, heart disease), household income, and depressive symptoms. Depressive symptoms were assessed using the Geriatric Depression Scale-15 (GDS)[18], a 15-item inventory in a yes/no format. Depressive symptoms were defined as a GDS score ≥ 6[19]. Body mass index was calculated as weight (kilograms) divided by height (meters) squared. Systolic and diastolic blood pressure, measured once, were assessed following standard methods. Total cholesterol, high-density lipoprotein, triglycerides, blood sugar, and hemoglobin A 1c were assessed using blood samples. Gait speed was assessed using a stopwatch; the participants were asked to walk 6.4 m (divided into two 2.0 m zones at each end and a 2.4 m middle zone) at their usual pace, and we measured the time required (in seconds) to complete the 2.4 m middle zone over two trials to calculate the mean gait speed (m/s). Mobility was assessed with a Timed Up and Go Test using a stopwatch. The participants were asked to stand up from a standard armchair, walk 3.0 m, then turn around, walk back to the chair, and sit down again. We measured the time required to complete the test. Handgrip strength was measured as muscle strength using a handgrip dynamometer (T. K.K. 5401; Takei Scientific Instruments, Niigata, Japan). One trial for each hand was performed, and the result from the stronger hand was used in the analysis.

Statistical analysis

The groups' baseline demographic and clinical characteristics were compared using the Fisher's exact test for categorical variables and unpaired t-test for continuous variables, as appropriate.

Intention to treat analyses were conducted using multivariate imputation by chained equations. Mixed effects models were developed to investigate the effect of the intervention program on cognitive function. The independent variables were allocation (categorical variable: intervention group and control group), time (categorical variable: baseline and follow-up), and the time by allocation interaction. Individual participants' intercepts for cognitive function were allowed to vary as random effects. Fifty imputed data sets were generated, and Rubin's rules were used to combine the results. Comparing with multivariate imputation analysis, complete case analysis was also applied.

Another mixed effects model was developed solely to investigate changes in cognitive function in the intervention group. The independent variable was time (categorical vari-

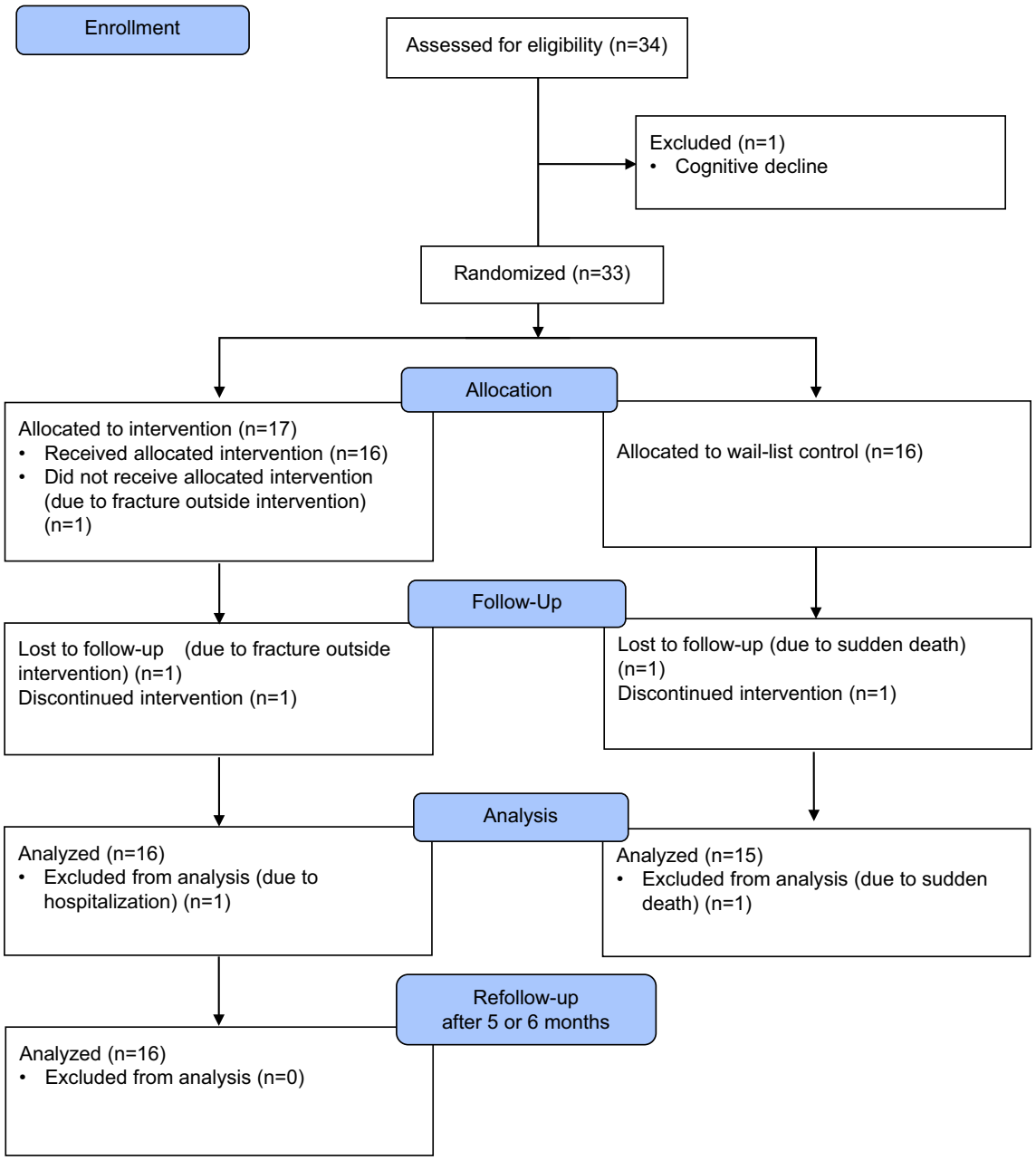

Fig. 1. Study Flow.

able: baseline, follow-up, and five months after intervention). The random effects of the intercept were also entered. Both multivariate imputation analysis and complete case analysis were applied.

All linear mixed effects models were calculated using the lmer function of lme4 package[20], and multivariate imputation by chained equations were conducted using mice package[21]. Statistical significance was set at $P < 0.05$, and all analyses were conducted using *R* (3.6.0).

Results

Demographic data

The baseline demographic and clinical characteristics of the two groups are depicted in Table 1. At baseline, there was no difference in cognitive function between the groups. The median (interquartile range) of the number of group activity participation is 10 (9-12). No adverse events were observed. Figure 1 depicts the flow of this trial. Two participants dropped out of this trial—one each in the intervention and control groups. The follow-up rate was 94%.

Effect of intervention on cognitive function

Table 2 presents the results of the mixed effects model with multivariate imputation by chained equations. The control group's MMSE score fell by 1.68 points, while in the intervention group, the score was maintained (0.00 points). No significant changes were observed in the other

Table 2. Effect of Exercise and Cognitive Activity on Cognitive Function: Mixed Effects Models

	Mean (Standard deviation)				Results of mixed effects model					
	Control group		Intervention group		Difference baseline value for intervention group (allocation)		Mean decline in outcomes in control group (time)		Additional decline in outcomes in intervention group (interaction)	
	Base-line	Fol-low-up	Base-line	Fol-low-up	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*
MMSE	28.47 (1.73)	26.73 (2.15)	27.38 (1.93)	27.44 (2.00)	-1.03 (-2.34 to 0.28)	0.122	-1.68 (-2.89 to -0.48)	0.007	1.68 (0.02 to 3.35)	0.048
TMT-A	44 (11.96)	41.06 (12.36)	45.35 (10.06)	42.28 (9.22)	0.94 (-6.5 to 8.38)	0.801	-2.94 (-7.65 to 1.77)	0.216	-0.12 (-6.68 to 6.44)	0.971
TMT-B	118.97 (47.74)	106.71 (44.03)	110.68 (66.18)	103.65 (32.72)	1.14 (-30.71 to 32.98)	0.943	-12.35 (-32.63 to 7.92)	0.228	-2.62 (-30.87 to 25.63)	0.854
DSST	44.73 (10.57)	44.67 (13.24)	44.94 (10.27)	47.69 (8.14)	-1.25 (-8.81 to 6.32)	0.743	0.02 (-3.14 to 3.19)	0.988	2.65 (-1.77 to 7.06)	0.235
WMS-R long-term	7.87 (4.12)	9.47 (5.32)	6.81 (3.78)	8.31 (3.53)	-0.34 (-3.42 to 2.75)	0.829	1.6 (-0.26 to 3.45)	0.09	-0.09 (-2.68 to 2.49)	0.942
WMS-R short-term	10.6 (4.56)	11.6 (5.03)	7.62 (3.84)	10.81 (3.82)	-2.43 (-5.43 to 0.57)	0.11	1.07 (-0.65 to 2.79)	0.218	2.06 (-0.34 to 4.45)	0.092

Abbreviations: 95% CI, 95% confidence interval; MMSE, Mini-Mental State Examination, TMT, Trail Making Test; DSST, Digit Symbol Substitution Test; WMS-R, Logical Memory Subtest of the Wechsler Memory Scale Revised. The mixed effects models were built using multiple imputation and means (standard deviations) were calculated using complete case data. There were three missing value in TMT-B at the follow-up assessment (Intervention Group: 2, Control Goup: 1), other outcome variables at follow-up had two missing value (Intervention Group: 1, Control Group: 1).

outcome models. Table S2 also showed similar results using complete case analysis. Figure S1 depicts changes in cognitive function.

Change in cognitive function in intervention group

Table 3 presents the results of the mixed effects model with multivariate imputation by chained equations to investigate changes in cognitive function in the intervention group. A significant improvement in long-term memory was observed in the intervention group at five or six months after the conclusion of the intervention. A significant improvement in short-term memory was observed in the intervention group at follow-up and five or six months after the conclusion of the intervention. Table S3 presents the results of the mixed effects model with complete case to investigate changes in cognitive function in the intervention group. A significant improvement in long-term and short-term memory was observed in the intervention group at follow-up and five or six months after the conclusion of the intervention.

Discussion

Our study investigated the effect of a combination of exercise and cognitive activity on cognitive function in community-dwelling older adults. As per the results, the decline in MMSE scores in the intervention group was lower than in the control group. Improvements in long-term and short-term memory were observed in the intervention group at follow-up and five months after the intervention as compared to the baseline.

Some randomized controlled trials have demonstrated the effect of the combination of exercise and cognitive activity on cognitive function[10]. Two randomized controlled trials in Japan reported higher cognitive function improvement in dual-task exercise groups than control groups[11,12]. The intervention contents in the present trial included a combination of cognitive activity and physical exercise, which helped in the maintenance of cognitive function as assessed using the MMSE. In previous combination studies of exercise and cognitive activity, cognitive activity was conducted either with or without exercise. In the present study, cognitive activity was conducted both with and without exercise, since the dual-task approach may be more efficacious than these activities conducted separately and cognitive activity homework is easy to implement[10]. The results of our study are in line with those of previous randomized controlled trials, aiding in the accumulation of insight into the combination effect on cognitive function.

Our result also suggested improvements in long-term and short-term memory in the intervention group at follow-up or five months after the intervention as compared to the baseline. Our intervention included memory training in dual-task exercises and cognitive activity homework, which might lead to the improvement of memory ability. However, this improvement was only observed in the pre-post

Table 3. Change in Cognitive Function in Intervention Group: Mixed Effects Models

	Mean (standard deviation)			Results of mixed effects model			
				Difference in predicted value between baseline and follow-up		Difference in predicted value between baseline and 5 or 6 months after intervention	
	Baseline	Follow- up	5 or 6 months after intervention	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*
MMSE	27.38 (1.93)	27.44 (2.00)	28.27 (1.53)	0.03 (-1.15 to 1.21)	0.96	0.84 (-0.36 to 2.04)	0.163
TMT-A	45.35 (10.06)	42.28 (9.22)	39.85 (12.81)	-2.79 (-8.39 to 2.80)	0.319	-4.49 (-10.11 to 1.13)	0.114
TMT-B	110.68 (66.18)	103.65 (32.72)	103.25 (21.71)	-12.96 (-35.03 to 9.12)	0.243	-15.12 (-37.1 to 6.86)	0.172
DSST	44.94 (10.27)	47.69 (8.14)	45.47 (7.74)	2.98 (-0.03 to 5.99)	0.053	0.73 (-2.38 to 3.85)	0.637
WMS-R long-term	6.81 (3.78)	8.31 (3.53)	9.60 (3.40)	1.20 (-0.39 to 2.78)	0.134	2.47 (0.85 to 4.08)	0.004
WMS-R short-term	7.62 (3.84)	10.81 (3.82)	10.73 (3.37)	2.94 (1.03 to 4.86)	0.003	3.03 (1.08 to 4.98)	0.003

Abbreviations: 95% CI, 95% confidence interval; MMSE, Mini-Mental State Examination; TMT, Trail Making Test; DSST, digit symbol substitution test; WMS-R, logical memory of the Wechsler Memory Scale Revised. The mixed effects models were built using multiple imputation and means (standard deviations) were calculated using complete case data. There were two missing value in the TMT-B at follow-up assessment, another outcome variable at follow-up has one missing value.

comparison. Therefore, our study could not conclude that this intervention caused memory improvement. Further studies should be conducted to clarify the long-term effects of the combination intervention by comparison to the control group.

In this trial, group activity was conducted once a week. In addition, participants had to do homework related to cognitive activity twice a week; thus, participants received intervention thrice a week. This increased the efficacy of our intervention without any additional effort on the part of the researchers. A previous meta-analysis reported that interventions with a frequency of five times or more per week have a greater effect on cognitive function than interventions with a frequency of four times or under per week[10]. Therefore, there is a need for studies that conduct more frequent interventions using homework.

Despite its contributions, this study has several limitations. First, the small sample size led to low statistical power. Estimated values in this sample may also be far from the true values of population. Our results suggested that MMSE decline in the control group was about 1.7, which is relatively larger than that of previous studies[11]. Attention should be paid to this point. However, it is noteworthy that through the insight it has accumulated, our study can be included in meta-analyses on this topic. Second, although it was not possible in this scenario, the lack of blinding of participants, supervisors, and assessors may have led to some bias. Third, the adherence to homework completion could not be measured as we could not observe it.

Conclusion

In conclusion, our results revealed that the decline in MMSE scores in the intervention group was lower than in the control group. Combining exercise and cognitive activity can be helpful for preserving cognitive function in healthy older adults.

Conflict of Interest: The author reports no conflicts of interest in this work.

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Supplementary material (Appendix):

1. Figure S1 Change in Cognitive Function By Group
2. Table S1 CONSORT 2010 checklist of information to include when reporting a randomised trial
3. Table S2 Effect of Exercise and Cognitive Activity on Cognitive Function: Mixed Effects Models with complete case
4. Table S3 Change in Cognitive Function in Intervention Group: Mixed Effects Models with complete case

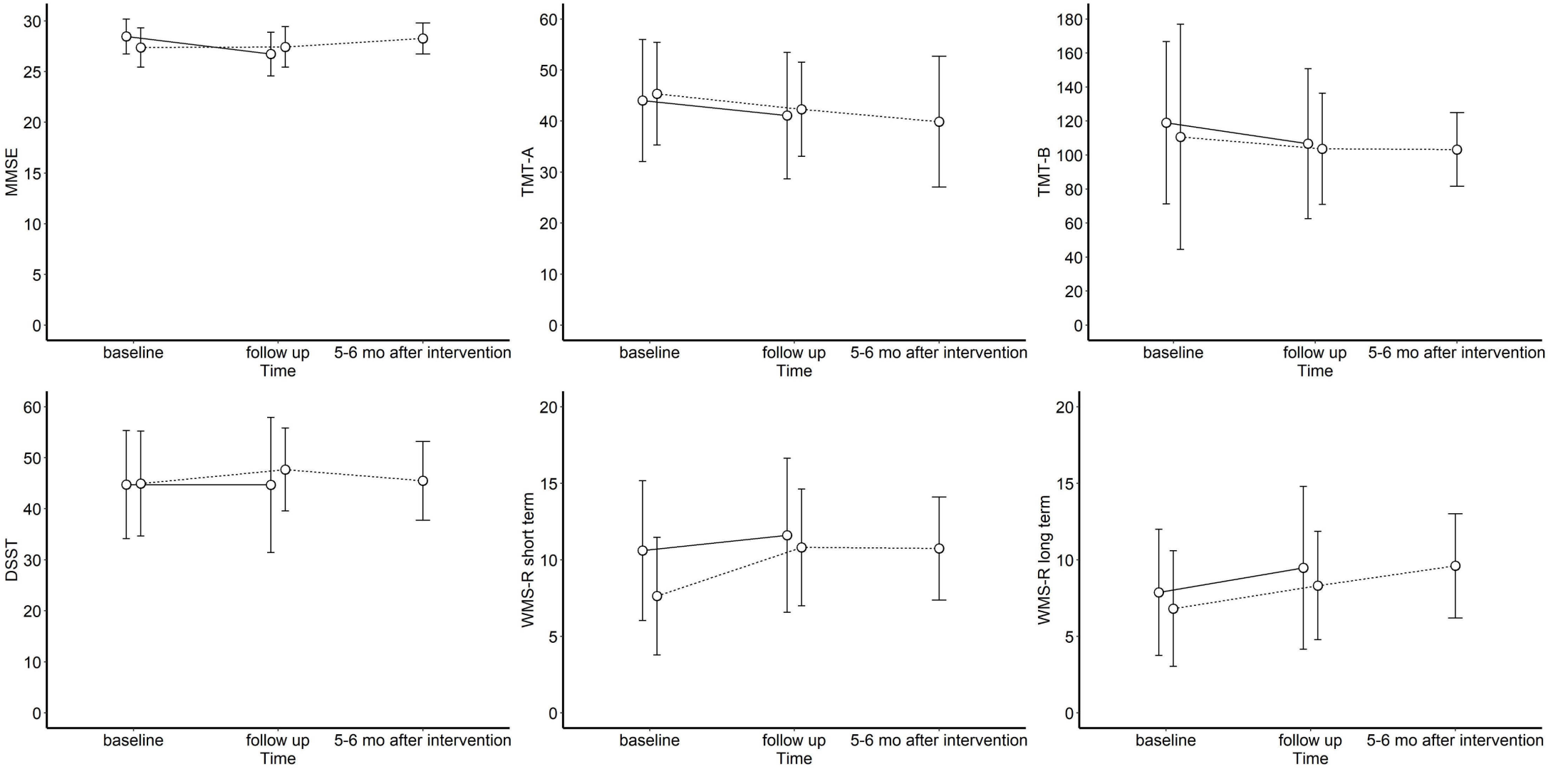

Fig S1. Change in Cognitive Function By Group.
Each graph shows mean and standard deviation. The dotted line represents the intervention group, and the solid line represents the control group. MMSE, Mini-Mental State Examination; TMT, Trail Making Test; DSST, digit symbol substitution test; WMS-R, Logical Memory Subtest of the Wechsler Memory Scale Revised.

Table S1. CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported in section
Title and abstract			
	1a	Identification as a randomised trial in the title	Title
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Abstract
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	Introduction
	2b	Specific objectives or hypotheses	Introduction
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Methods
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Methods
Participants	4a	Eligibility criteria for participants	Methods
	4b	Settings and locations where the data were collected	Methods
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Methods
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Methods
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Methods
Sample size	7a	How sample size was determined	n/a
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	Methods
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Methods
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Methods
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Methods

Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Methods
	11b	If relevant, description of the similarity of interventions	Methods
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Methods
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Methods
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Results
	13b	For each group, losses and exclusions after randomisation, together with reasons	Results
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Methods
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Results
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results, Table 2
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n/a
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Results
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Results
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Discussion
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Discussion
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Discussion
Other information			
Registration	23	Registration number and name of trial registry	Trial Registration
Protocol	24	Where the full trial protocol can be accessed, if available	n/a
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Acknowledgments

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Table S2 Effect of Exercise and Cognitive Activity on Cognitive Function: Mixed Effects Models with complete case

	Results of mixed effects model					
	Difference baseline value for intervention group (allocation)		Mean decline in outcomes in control group (time)		Additional decline in outcomes in intervention group (interaction)	
	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*
MMSE	-1.09 (-2.45 to 0.26)	0.114	-1.73 (-2.97 to -0.5)	0.008	1.80 (0.07 to 3.52)	0.043
TMT-A	1.35 (-6.26 to 8.96)	0.724	-2.94 (-7.85 to 1.97)	0.236	-0.13 (-6.97 to 6.71)	0.970
TMT-B	-1.00 (-34.78 to 32.79)	0.953	-12.26 (-33.79 to 9.26)	0.258	-2.88 (-33.32 to 27.57)	0.850
DSST	0.20 (-7.25 to 7.66)	0.956	-0.07 (-3.37 to 3.23)	0.968	2.82 (-1.78 to 7.41)	0.224
WMS-R long-term	-1.05 (-3.99 to 1.89)	0.477	1.60 (-0.33 to 3.53)	0.105	-0.10 (-2.79 to 2.59)	0.941
WMS-R short-term	-2.98 (-5.99 to 0.04)	0.054	1.00 (-0.79 to 2.79)	0.267	2.19 (-0.3 to 4.68)	0.086

Abbreviations: 95% CI, 95% confidence interval; MMSE, Mini-Mental State Examination, TMT, Trail Making Test; DSST, Digit Symbol Substitution Test; WMS-R, Logical Memory Subtest of the Wechsler Memory Scale Revised. Sample size of the models was 31 (intervention group:16, control group:15) except for that of TMT-B outcome model due to missing value [30 (intervention group:15, control group:15)].

Table S3 Change in Cognitive Function in Intervention Group: Mixed Effects Models with complete case

	Results of mixed effects model			
	Difference in predicted value between baseline and follow-up		Difference in predicted value between baseline and 5 or 6 months after intervention	
	Estimate (95% CI)	*p*	Estimate (95% CI)	*p*
MMSE	0.06 (-1.17 to 1.29)	0.919	0.91 (-0.35 to 2.15)	0.151
TMT-A	-3.07 (-8.78 to 2.65)	0.286	-5.01 (-10.89 to 0.79)	0.092
TMT-B	-7.03 (-32.79 to 18.72)	0.585	-8.66 (-34.8 to 17.78)	0.510
DSST	2.75 (-0.30 to 5.80)	0.078	0.34 (-2.77 to 3.46)	0.827
WMS-R long-term	1.50 (0.04 to 2.96)	0.047*	2.97 (1.46 to 4.46)	<0.001
WMS-R short-term	3.19 (1.34 to 5.04)	0.002**	3.38 (1.47 to 5.26)	0.001

Abbreviations: 95% CI, 95% confidence interval; MMSE, Mini-Mental State Examination; TMT, Trail Making Test; DSST, digit symbol substitution test; WMS-R, logical memory of the Wechsler Memory Scale Revised. Sample size of the models was 16 except for that of TMT-B outcome model due to missing value (N=15).

PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Effect of Home-based Exercise Therapy for Peripheral Arterial Disease Patients Underwent Endovascular Treatment: A Clinical Controlled Design

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ABSTRACT. Objective: This study aimed to clarify the effect of home-based exercise therapy on physical activity in peripheral arterial disease (PAD) patients after EVT. Methods: Study design was controlled clinical design. The subjects were 30 patients (76.6% men) who underwent EVT in the Sakakibara Heart Institute of Okayama. Patients with EVT meeting the inclusion criteria were divided into two groups, intervention group (Home-based exercise) and control group. Patients' basic characteristics, the number of steps walked and QOL questionnaire (WIQ, SEPA, Vascu QOL) were assessed before surgery and, at the 3 month after discharge. A two-way analysis of variance (ANOVA) was performed to compare number of steps walked and QOL questionnaire. Results: Interaction effect were observed in the number of steps walked ($F(1,28) = 13.89$, $p<0.01$). A multiple comparison test confirmed a significant increase between results of before surgery and at three months after surgery in the intervention group ($p<0.01$). An interaction between the presence and absence of intervention was found for the WIQ pain score ($F(1,28) = 5.86$, $p=0.01$), speed score ($F(1,28) = 3.80$, $p=0.04$) and SEPA ($F(1,28) = 4.99$, $p=0.03$). In a multiple comparison study, there was a significant increase in WIQ pain and speed scores in both groups before and 3 months after discharge from the hospital. Conclusion: Home-based exercise therapy using physical activity indices has the potential to improve number of steps and quality of life in patients with PAD after EVT.

Key words: Home-based exercise, Peripheral arterial desease, Endovascular treatment, Physical activity

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Peripheral arterial disease (PAD) is treated differently depending on the severity of the condition. Endovascular treatment (EVT) is the first choice for patients with symptomatic PAD in the Transatlantic Inter-Society Consensus (TASC) classification[1)]. In addition, EVT is a minimally invasive and safe treatment method that is rapidly increasing[2)]. However, due to its benefits, many patients have a short hospital stay and do not receive adequate exercise during their hospital stay. In our previous study, the combination of EVT and exercise therapy during hospitalization resulted in a significant 286% improvement in maximum walking distance, but not a significant 127% improvement in number of steps[3)]. This report showed difficulty in obtaining a regular exercise routine after EVT.

PAD patients have a lower amount of physical activity, compared to healthy people. Previous studies have reported that the average number of steps within daily life for PAD patients with intermittent claudication is 3000-4000 steps/day[4-6)]. Patients with low physical activity in PAD are also at higher risk for worsening PAD and developing cardiovascular events[7)]. Garg et al[8)] examined cardiovascular mortality at 57 months in four groups of patients with PAD

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according to physical activity level. It was reported that the group with the lowest physical activity level had twice the cardiovascular mortality rate than the group with the highest physical activity level. Therefore, it has been suggested that the management of physical activity is extremely important for patients with PAD in terms of prognosis, including PAD exacerbations and cardiovascular mortality[9-12]. Furthermore, it has been reported that increased physical activity affects the promotion of quality of life in patients with PAD[13], suggesting that there is an important relationship between physical activity and quality of life.

For this reason, home-based exercise therapy has recently been attracting attention as a treatment method for patients with PAD. Daily recording, quantification of physical activity using a triaxial accelerometer, strict setting of exercise intensity, and frequent feedback are necessary for the success of home exercise therapy in patients with PAD[14,15]. McDermott et al[16] compared the control group with the home-based exercise group and reported that at 6 months, the home-based exercise group improved physical activity by 11%, WIQ distance score by 34%, and WIQ speed score by 32% from baseline.

Despite the above reports, no studies have reported the effect of home-based exercise on physical activity in PAD patients after EVT, which has been on the rise in recent years. This study aimed to clarify the effect of home-based exercise therapy on physical activity in PAD patients after EVT.

Methods

Trial design

This study was a prospective, single-center, two-arm, controlled clinical design. In the present study, the eligibility criteria for patients with PAD were those who underwent EVT according to the TASC classification. 84 consecutive PAD patients who underwent EVT between August 2016 and December 2017 participated in the protocol of this study. The TASC classification is defined by the location and distribution of the lesion, which may result in bias in patient performance. Therefore, based on previous studies, the exclusion criteria for this study were established as follows[14,15]. The following exclusion criteria were applied: (1) unable to walk independently before EVT; (2) diagnosis of dementia; (3) lower extremity amputation; (4) critical limb ischemia; (5) not responding to the post-discharge survey; and (6) missing data.

Outcome

The primary outcome of the study was the change in the number of steps from pre-EVT to 3 months after discharge from the hospital. Secondary outcomes included changes in the following parameters: WIQ, SEPA and Vascu QOL.

Measurement of physical activity and analysis method

Physical activity was measured using a triaxial accelerometer (Active style Pro HJA-750C, Omron Co. Japan). A triaxial accelerometer was worn daily from the time of the outpatient visit when the patient was diagnosed with the need for surgery until three months after discharge from the hospital (excluding the hospitalization period), and the number of steps walked was recorded. Patients were instructed to wear a triaxial accelerometer on their lower back throughout the day, from waking up to bedtime, except when bathing or going to bed. The average number of steps was calculated from data that excluded days in which wear time was less than 480 minutes/day for any reason[17]. The percentage change in steps walked before and at 3 months after surgery was calculated so that individual differences in step count could be taken into account and the effectiveness of home exercise could be evaluated. The following formula was used to calculate the rate of change: (average steps at 3 months after discharge minus average preoperative steps) / x 100.

Evaluation of QOL

The following questionnaires were measured before hospitalization and at 3 months post-discharge; Walking Impairment Questionnaire (WIQ)[18] to evaluate the ability to walk; Self-Efficacy for Physical Activity (SEPA)[19] to evaluate subjective self-efficacy; Vascular Quality of Life Questionnaire (Vascu QOL)[20] to evaluate ADL of patients with PAD. For the post-discharge quality of life assessment, the questionnaire was mailed to the patient and the patient completed the questionnaire and returned it to us.

Evaluation hemodynamics, exercise tolerance and physical function

The following items were measured before and after admission and before discharge for pre- and post-EVT assessment. Ankle Brachial Pressure Index (ABI) to evaluate hemodynamics; 6-minute walk distance (6MWD) to evaluate exercise tolerance; Short Physical Performance Battery (SPPB) to evaluate physical function. 6MWD was measured according to the American Thoracic Society (ATS) guidelines[21] before EVT and before hospitalization. Patients were asked to walk back and forth for 6 minutes with assistance between two markers placed at 30 m intervals on flat ground, and their walking distance was measured.

Rehabilitation intervention after endovascular treatment (exercise therapy and pre-discharge instructions)

After EVT, all patients began standing and walking exercises the day after surgery. When the patient was able to walk independently on level ground without developing complications, exercise therapy with a treadmill was started. One treadmill exercise regimen consisted of a warm-up, a 20-minute treadmill walk, and a cooling down.

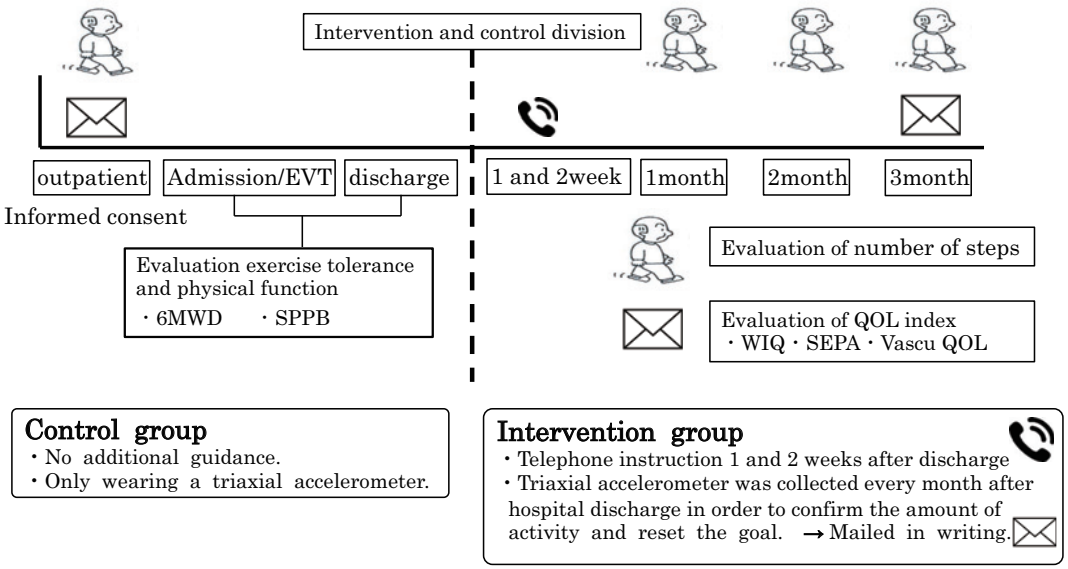


Fig. 1. study protocol

Table 1. Instruction for intervention group

Walking steps	① Increase of 1300 steps/day. (guidelines of Physical Activity and Exercise by MHLW)
	② Mean number of steps walked in each age bracket.
	③ Goal of older patients. Male 6700 steps, Female 5900 steps.
	※ Goal was achieved shift to next aim.
Time	・30 ～ 45 min/1 session
Walking method	・Do comfortable walking speed
	・The patient should stop walking when claudication pain is considered moderate (over Borg scale 15).

This was performed while the patient was in the hospital. The exercise prescription for treadmill-based exercise therapy was in line with the Trans-Atlantic Inter-Society Consensus II (TASC II)[1], an international treatment guideline for PAD. The walking speed and load were gradually increased as the ability to walk improved. The mean number of days of exercise therapy was 5.32 days (range: 2-10 days). At discharge, all patients were instructed to aim to exercise at least three times a week for at least 30 minutes each time. Prior to discharge, the patient received regular exercise advice from the doctor, medication instructions from the pharmacist, and lifestyle guidance from the public health nurse, as well as ADL guidance to avoid excessive flexion at the stent insertion site. For the exercise therapy provided up to the day of discharge and the ADL instruction provided on the day of discharge, the control and intervention groups received the same level of therapeutic intervention. No patients in this study received outpatient rehabilitation after discharge from the hospital.

Randomization

A controlled clinical trial was used for this study. Patients were alternately assigned to the control and intervention groups.

Protocol in the control group and the intervention group

The exercise protocol for both groups is shown in Figure. 1. The follow-up period was 3 months after discharge from the hospital. After discharge, the protocol did not include additional instruction in the control group. They were also instructed to wear a triaxial accelerometer only. On the other hand, in the intervention group, the post-discharge protocol included instruction based on pre-admission steps and the Ministry of Health, Labour and Welfare's physical activity and exercise guidelines[22] (Table 1). The patient was instructed on the number of steps, the duration of walking, and how to walk. The initial goal was to increase the number of steps from the average number of steps taken before admission to the hospital to 1300 steps per day. Each time the goal was achieved, the goal was re-set based on the average number of steps in each age group and the target number of steps for the elderly. Based on previous studies[11,12,23], feedback was provided by telephone one to two weeks after discharge from the hospital, and a triaxial accelerometer was collected and results mailed every month after surgery. During the telephone consultations, we reviewed the advice received from other professionals prior to discharge and listened to whether they were practicing the advice and confirmed that they were continuing to exer-

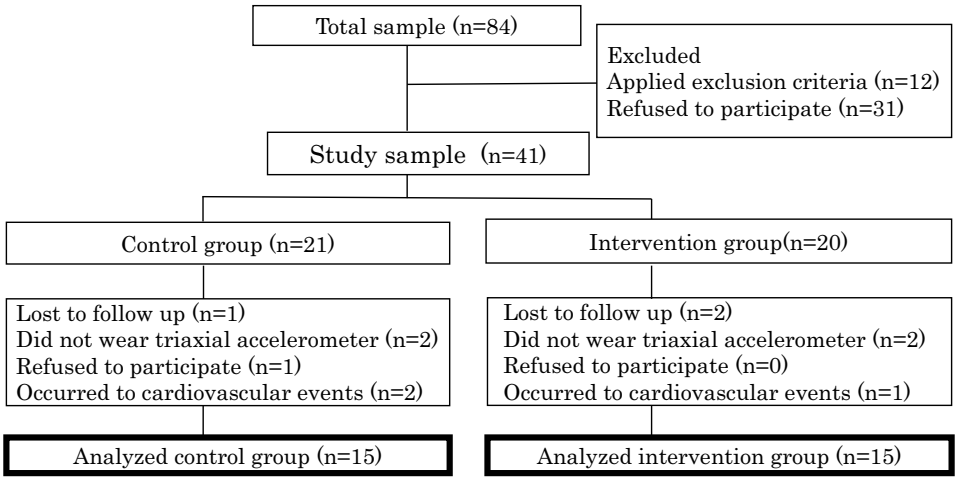


Fig. 2. study flowchart

cise. At the monthly mailing instruction, the triaxial accelerometer received was analyzed and the difference between the average and target steps was presented and the next goal was re-established. All interventions were also carried out by the same physiotherapist. As an evaluation of the implementation of exercise therapy, the rate of achievement of the initial goal at 3 months post-discharge was presented. The initial goal was an increase of 1300 steps/day from the mean number of steps before EVT, as described above.

Analytical methods and statistical methods

We used unpaired t-tests to compare the averages of continuous variables (such as age) and χ^2 tests to compare the proportions of categorical variables (such as sex) between the groups. Rates of change and median were compared using Wilcoxon rank-sum tests. Comparisons of ABI, 6MWD, and SPPB scores before and after EVT were performed using within-groups paired t-test and between-groups unpaired t-test. Comparisons between changes in number of steps and WIQ, SEPA, Vascu QOL were made using a two-way analysis of variance (ANOVA); if interactions were present, a multiple comparison test was used. In this study, the effect size was calculated in order to evaluate the magnitude of the difference. The ϕ coefficient was calculated as the effect size by the χ^2 test, and it was interpreted that ϕ=0.1 is small, ϕ=0.3 is medium, and ϕ=0.5 is large. The unpaired and paired t-tests calculated Cohen's d and interpreted that d=0.2 was small, d=0.5 was medium, and d=0.8 was large. For Wilcoxon rank sum test and Mann-Whitney U test, r was calculated and interpreted as r =0.1 is small, r=0.3 is medium, and r=0.5 is large. For two-way analysis of variance, η^2 was calculated and η^2=0.01 was small, η^2=0.06 was medium, and η^2=0.14 was large. All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY). The threshold for significance was $p<0.05$.

Ethical considerations

This study was conducted in accordance with the Helsinki Declaration and was approved by the ethical committee of Hyogo University of Health Sciences (approval number: 16021) and the ethical committee of the Sakakibara Heart Institute of Okayama (approval number: 20140901).

Results

Study population

After the study criteria were applied, the remaining 41 patients participated in the study and 41 patients were alternately assigned to the control (n=21) and intervention (n=20) groups. Among them, 15 in the control group and 15 in the intervention group, who were able to continue wearing the triaxial accelerometer 3 months after surgery, proceeded to analysis (Fig. 2).

Comparison of basic information between the control group and the intervention group

There were no deaths during hospitalization. All patients were discharged home after surgery, with a mean hospital stay of 6.8 days (range: 2-12 days). The mean number of days to triaxial accelerometer data collection was 15.2 days before admission (range, 7-30) and 58.6 days 3 months after discharge (range, 30-84). A comparison of the basic information between the control and intervention groups is shown in Table 2. There was no significant difference between the two groups in terms of basic information and past medical history.

Pre-surgery and post-surgery comparison of the therapeutic areas, hemodynamics, exercise tolerance and physical function between the control group and the intervention group

A comparison of the treatment area, hemodynamics, exercise tolerance and physical function of the control and

Table 2. Comparison of patient's characteristics between the control group and the intervention group

	Control group (n=15)	Intervention group (n=15)	p value	Effect size
Average age (range)	74.4 (66-81)	73.2 (70-80)	0.48	0.27
Sex (male/female) *	12/3	11/4	0.67	0.08
BMI (AVG±SD)	24.0±3.8	22.6±2.9	0.31	0.41
Smoking*	13 (86.7)	14 (80.0)	0.54	0.11
Fontaine classification (stage II/stage III)	14/1	13/2	0.54	0.11
Past history n (%)				
Hypertension*	15 (100.0)	13 (86.7)	0.14	0.27
Dyslipidemia*	15 (100.0)	13 (86.7)	0.14	0.27
Chronic kidney disease*	8 (53.3)	9 (60.0)	0.71	0.07
Diabetes mellitus*	8 (53.3)	9 (60.0)	0.71	0.07
Coronary artery disease*	10 (66.7)	9 (60.0)	0.70	0.07
Cerebral vascular disease*	4 (26.7)	5 (33.3)	0.69	0.07
Orthopedic disorder*	5 (33.3)	4 (26.7)	0.69	0.07

BMI; Body mass index, *: χ^2 test

intervention groups is shown in Table 3. There was no significant difference between the two groups in terms of therapeutic area. Significant improvements in ABI were observed within both groups, but there were no significant differences between the two groups. There was no significant difference in the rate of change in 6MWD between the two groups. Similarly, there was no significant difference in SPPB between the two groups.

Pre-surgery and post-surgery comparison of the number of steps walked and the rate of change in the number of steps walked

Interaction effects were observed with the number of walking steps and with or without intervention ($F(1,28) = 13.89$, $p<0.01$). In a multiple comparison test, a significant increase was observed between before surgery and at three months after discharge in the intervention group (3162.1± 1439.9 vs. 4503.7±1768.6; $p<0.01$) (Fig. 3). In addition, a significantly high rate of change in the number of steps walked was observed in the intervention group at three months after discharge (13.4% vs. 46.5%; $p<0.01$). Initial goal attainment was significantly higher in the intervention group (20.0% vs 53.3%; $p<0.01$).

Pre-surgery and post-surgery comparison of QOL indexes

An interaction between the presence and absence of intervention was found for the WIQ pain score ($F(1,28) = 5.86$, $p=0.01$), speed score ($F(1,28) = 3.80$, $p=0.04$) and SEPA ($F(1,28) = 4.99$, $p=0.03$) (Table 4). In a multiple comparison study, there was a significant increase in WIQ pain and speed scores in both groups before and 3 months after discharge from the hospital.

Between the two groups, the WIQ pain score and speed score were significantly increased in the intervention group 3 months after surgery. (Pain score: 61.6±22.1 vs 83.3±21.7, $p<0.05$; speed score: 55.2±20.5 vs 70.4±16.8, $p<0.05$). A significant increase in SEPA was found only in the intervention group before and 3 months after discharge (42.6±27.6 vs 53.8±25.4; $p<0.05$).

Discussion

A comparison of the primary outcome of this study, the number of steps, showed a significant difference between the intervention group at the preoperative and 3 months after discharge. In addition, when the rate of change in the number of steps taken before and 3 months after discharge was compared between the two groups, a significantly higher value was observed in the intervention group. Previous studies have shown mixed results on the effects of short-term home exercise therapy on physical activity in patients with PAD. McDermott et al[14] reported that after 6 months of home-based exercise for PAD patients with intermittent claudication, there was an 11% increase in physical activity from baseline and a significant improvement compared to the control group. However, Gardner et al[15] reported that after 3 months of home-based exercise in patients with PAD, the number of steps increased by 10% from baseline, but there was no significant improvement compared to the control group and supervised exercise therapy group. In the present study, after 3 months of home-based exercise, the rate of change in the number of steps was significantly increased compared to the control group. he results may be related to two novelties in this study. The first is that the study's population was limited to EVT patients. Patients with PAD with low PA have been reported to be due to females, low education, high comorbidity, low ABI, low motor endurance, and low WIQ score[24-26]. In this study, the improvement in ABI and WIQ scores was observed with EVT revascularization, suggesting that home exercise may have been more effective than in previous studies. The second factor was setting specific goals for the

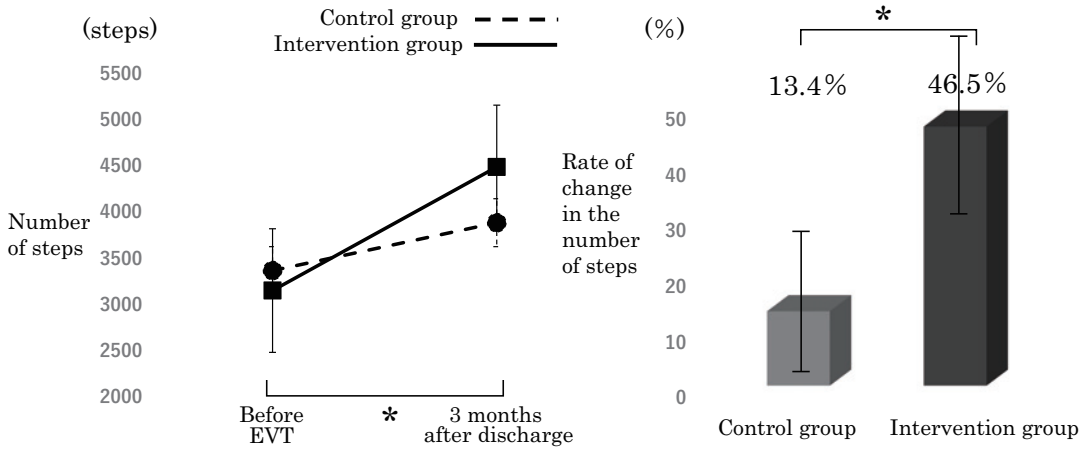
Table 3. Comparison of patient's therapeutic areas, hemodynamics, exercise tolerance and physical function between the control group and the intervention group

	Control group (n=22)	Intervention group (n=20)	p value	Effect size
Therapeutic regions※ (n=42)				
Iliac artery area/Femoral artery area*	14/8	13/7	0.93	0.01
ABI	(n=15)	(n=15)		
Before EVT (AVG±SD)	0.66±0.13 †	0.72±0.15 †	0.29	0.43
After EVT (AVG±SD)	1.02±0.11	0.98±0.13	0.74	0.33
6MWD	(n=15)	(n=15)		
Before EVT	292.0 (120.0-480.0)	321.6 (200.0-460.0)		
After EVT	342.8 (220.0-550.0)	372.5 (250.0-520.0)		
Change of rate (%)	117.4	115.8	0.67	0.08
SPPB	(n=15)	(n=15)		
Before EVT median (range)	12 (7-12)	12 (7-12)	0.56	0.08
After EVT median (range)	12 (8-12)	12 (8-12)	0.68	0.07

※ There are overlapping therapeutic regions.

ABI; ankle brachial index, EVT; endovascular treatment, 6MWD; 6-minutes walk distance, SPPB; short physical performance battery

*: χ^2 test, †: paired t-test vs Before EVT $p<0.01$



	Number of steps		
	Before EVT	3 months after discharge	Effect size
Control group	3378.5±1088.1	3898.8±974.5	0.50
Intervention group	3162.1±1439.9	4503.7±1768.6*	0.83

F value (Effect size η^2)		
Walking steps change	With or without an intervention	Interactive effect
19.90 (η^2=0.08) *	0.16(η^2=0.01)	13.89(η^2=0.06)*

*p<0.01

Fig. 3. Comparison of number of steps and rate of change in the number of steps
EVT; endovascular treatment

number of steps and periodically rescheduling the goals. The rate of achievement of the initial goal (1300 steps/day increase from the mean number of steps before EVT) was significantly higher in the intervention group. Because previous studies have shown that EVT, inpatient exercise therapy, and discharge instruction alone did not lead to an increase in steps, regular tele-teaching may have been effective in motivating subjects to exercise walking. The content of the guidance used in the intervention group in the current study was not a goal developed specifically for patients with PAD, but was originally developed by our team based on the physical activity and exercise guidelines of the MHLW[22]. Therefore, although the relevance of the instruction is unclear, the team believes that the team has been

Table 4. Comparison of patient's QOL indexes between the control group and the intervention group

	Before EVT		3 months after discharge		Main effect			interaction		
	Control group (n=15)	Intervention group (n=15)	Control group (n=15)	Intervention group (n=15)	F value	p value	Effect size (η^2)	F value	p value	Effect size (η^2)
WIQ (AVG±SD)										
Pain	43.3±24.9	34.7±23.0	61.6±22.1*	83.3±21.7**†	28.5	<0.01	0.32	5.86	0.01	0.07
distance	33.1±30.1	36.5±31.9	69.7±26.8	79.8±22.9	26.3	<0.01	0.32	0.18	0.66	0.01
speed	35.4±15.2	32.5±14.0	55.2±20.5*	70.4±16.8**†	39.0	<0.01	0.40	3.80	0.04	0.04
climbing	40.2±25.4	37.8±33.6	54.4±22.4	68.3±27.9	8.84	0.01	0.14	1.17	0.28	0.02
total	152.2±72.7	141.5±92.8	241.1±79.2	301.9±70.7	33.6	<0.01	0.37	2.76	0.10	0.03
SEPA (AVG±SD)	46.3±21.8	42.6±27.6	45.4±14.4	53.8±25.4**	7.76	0.01	0.12	4.99	0.03	0.08
Vascu QOL (AVG±SD)	103.0±39.5	108.3±41.6	133.4±28.2	152.5±14.1	21.0	<0.01	0.27	0.68	0.41	0.01

WIQ; walking impairment questionnaire, SEPA; self-efficacy for physical activity, Vascu QOL; vascular quality of life questionnaire, EVT; endovascular treatment

Wilcoxon rank-sum test: * vs. Before EVT control group $p<0.05$, ** vs. Before EVT intervention group $p<0.05$, †vs. 3 months after EVT intervention group $p<0.05$

successful in encouraging behavioral change in patients by setting specific steps in addition to periodically re-setting goals and providing guidance on how to achieve those goals.

Among the items that had a significant interaction with the presence or absence of the intervention, significantly higher WIQ pain and WIQ velocity scores were observed in the intervention group than in the control group 3 months after discharge. A significant increase in SEPA was also observed preoperatively and 3 months after surgery in the intervention group only. The combination of EVT and exercise therapy has been reported to improve walking distance and quality of life in both the short and long term compared to EVT and exercise therapy individually[27]. Furthermore, home-based exercise therapy has also been reported to improve quality of life indicators[28]. McDermott et al[16] reported a 34% increase in WIQ distance score and a 32% increase in WIQ speed score from baseline after 6 months of home exercise. The present study showed similar results. Increased SEPA and Vascu QOL have been reported in patients with PAD along with improved walking ability[29,30]. Quality of life and self-efficacy of the patients in this study may also have improved as the number of steps increased, although an increase in the number of steps is not equal to an increase in walking ability.

There are several limitations to this study. First, due to insufficient numbers of patients, it was not possible to perform a proper statistical analysis of changes in the number of steps walked. Therefore, the effect sizes were tested retrospectively, but the effect sizes for the primary outcome were moderate. Secondly, participation was also very limited because some subjects did not consent to the study and some withdrew from the study. Therefore, the majority of participants are considered to be highly compliant with the exercise. Third, several patients in the intervention group failed to achieve the initial goal of 1300 steps/day from their pre-hospitalization step count. Because these patients were included in the analysis, not all subjects in the intervention group were able to perform the home-based exercise targeted in this study. Finally, the results show only short-term effects, and the medium- to long-term effects are unknown.

Conclusion

In summary, home-based exercise therapy using physical activity indices improves number of steps and quality of life for PAD patients after EVT. Our findings suggest that providing personalized, home-based exercise therapy may help PAD patients with PAD to develop regular physical exercise habits after discharge from hospital.

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Conflict of Interest: The authors declare that we have no competing interests.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Psoas Muscle Volume and Attenuation are Better Predictors than Muscle Area for Hospital Readmission in Older Patients after Transcatheter Aortic Valve Implantation

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ABSTRACT. Objective: This study aimed to determine whether the psoas muscle volume (PMV) and its muscle attenuation (MA) are associated with hospital readmission after transcatheter aortic valve implantation (TAVI). Method: We included 113 older patients with aortic stenosis who underwent TAVI at Sakakibara Heart Institute (mean age 85 ± 5 years, 69% women). We measured PMV and psoas muscle area (PMA) as well as total muscle area (TMA) at the third lumbar vertebra using preoperative computed tomography (CT) images. The crude values of the PMV, PMA, and TMA were normalized by dividing by height squared. Results: The median follow-up period was 724 days (interquartile range: 528-730 days), and there were 25 all-cause readmissions during the follow-up period (22% of all patients). In the multivariate Cox regression analysis adjusted for age, sex, and EuroSCORE II, the PMV and its MA and crude PMA were significantly associated with all-cause readmission [HR: 0.957 (0.930-0.985), p = 0.003, HR: 0.927 (0.862-0.997), p = 0.040], whereas the PMA and TMA and each MA were not (all p > 0.05). The groups with low PMV and MA had significantly higher incidences of all-cause readmission than that with high PMV and MA (log-rank test: p = 0.011). Conclusion: PMV and its MA measured from preoperative CT images were independent predictors of all-cause readmission in TAVI patients.

Key words: Muscle mass, Sarcopenia, Transcatheter aortic valve implantation, Aortic stenosis, Readmission

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The incidence of aortic stenosis increases with age, and the number of surgical operations for aortic stenosis has increased with the aging of the population[1,2]. Patients with severe aortic stenosis who are at high risk for surgery, including older patients and those with comorbidities, are chosen to undergo transcatheter aortic valve implantation (TAVI). Readmissions after TAVI are relatively frequent, and readmissions within one year after TAVI occur at a frequency of approximately 20-50%[3]. Preventing readmission is an important issue for maintaining quality of life and reducing health care costs.

Low muscle mass or sarcopenia are a prognostic factor for all-cause mortality in patients with cardiac disease, including patients undergoing TAVI[4,5]. In these patients, the percentage of those with low muscle mass, as determined by the cutoffs of previous studies, was reported to be around 60%[5-7]. In elderly patients admitted to the acute care ward, the diagnosis of sarcopenia, including low muscle mass, has been reported to increase readmission rates after discharge[8]. Nevertheless, it is unclear whether low muscle mass predicts readmission in patients who undergo TAVI.

Reports of muscle mass measured using computed tomography (CT) have increased in recent years. The measurement site for the evaluation of muscle mass is usually the cross-sectional area of the total skeletal muscle or the psoas muscle at the third lumbar vertebra (L3)[9,10]. In pa-

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tients with major vascular disease, the risk of all-cause mortality was greater in groups with smaller cross-sectional area in the total skeletal muscle and psoas muscle at L3 than in those with larger areas[11,12].

The European Working Group on Sarcopenia in Older People reported that the total skeletal muscle and the psoas muscle at the L3 measured using CT require further verification to be used for sarcopenia evaluation[13]. Because patients under undergo TAVI are elderly and often have spinal deformations, there may be limits to assessing muscle mass in one cross section. In elderly patients with substantial spinal deformations, the volume of the psoas muscle on CT may be evaluated more accurately than measurements of cross-sectional area. There are reports of measurements of muscle mass using volume in other fields such as oncology, and the relationship with prognosis has also been reported[14,15]. Nevertheless, there are few reports of patients with cardiac disease, including patients undergoing TAVI. Reports on the assessment of muscle quality using CT values are increasing, and the attenuation of muscle quality is reportedly associated with a decline in physical function and prognosis[16,17]. Assessing muscle mass and quality deterioration using standard pre-TAVI protocol may lead to early identification of the risk of worse outcomes, and early referral to physical therapy. Therefore, this study aimed to determine whether psoas muscle volume (PMV) and its muscle attenuation (MA) are associated with all-cause hospital readmission after TAVI.

Methods

Study population

This study was conducted at a single center, and the study design was retrospective. The study included 116 consecutive patients with aortic stenosis who underwent TAVI at the Sakakibara Heart Institute between 2016 January and 2017 March. We excluded three patients who had undergone spinal fusion surgery in the past because implanted orthopedic hardware caused metal artifacts. This study was approved by the ethics board of the Sakakibara Heart Institute (ID: 18-011), and written informed consent was obtained from all patients. Study procedures were carried out in accordance with the Declaration of Helsinki and the Ethical Guidelines for Medical and Health Research Involving Human Subjects (Japanese Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare).

Assessment of physical function

Grip strength was used to evaluate the maximum muscle strength and was measured using a handgrip dynamometer. Patients were measured in a sitting position with elbow flexion of 90 degrees, 3 times on each side. Grip strength was calculated by averaging the maximum values of the left and right sides. Gait speed was calculated by dividing 4 m by the time required to walk the distance. Patients were instructed to walk at a comfortable speed and were allowed to use walking aids such as canes and walkers. Patients unable to walk the distance were recorded as having a gait speed of 0 m/sec.

Assessment of skeletal muscle in CT images

PMV, psoas muscle area (PMA), and total muscle area (TMA) were obtained from preprocedural CT images. The PMV, PMA, and TMA were measured using semi-automatic methods on Ziostation2 (Ziosoft, Tokyo, Japan), as shown in Figure. 1. The PMV was measured from the level of the lumbar vertebra to the plane connecting the bilateral anterior superior iliac spine in the sagittal axis (Fig. 1A, 1B). The PMA and TMA were analyzed in the cross-sectional area in the axial plane at the middle of L3 (Fig. 1C, 1D). In the selected PMV, PMA, and TMA, thresholds of CT values were -30 to +150 Hounsfield Units (HU) because of the exclusion of fat or other tissues except for the muscle. The PMV and PMA were calculated as the sum of the left and right psoas muscles. The crude values of the PMV, PMA, and TMA were normalized by dividing by height squared. To evaluate the MA, average CT values were evaluated in the measured PMV, PMA, and TMA. The measurements of skeletal muscle were made by an independent observer. To evaluate interobserver agreements for the measurements, the intraclass correlation coefficient (ICC) was used in the analysis of randomly selected 20 patients by two independent observers. The ICCs for the PMV, PMA, and TMA were 0.984, 0.989, and 0.989, respectively, and the ICCs for the MA of the PMV, PMA, and TMA were 0.997, 0.975, and 0.972, respectively.

Endpoint and follow-up

The endpoint of this study was unplanned all-cause readmission following TAVI. We obtained follow-up data from medical records or by telephone interviews. The follow-up period was a maximum of two years.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation for normal distribution or median (interquartile range: 25^{th} to 75^{th} percentiles) for non-normal distribution, and categorical variables are expressed as numbers or percentages. The distribution of each continuous variable was assessed for normality using the Shapiro-Wilk test. Comparisons between gender in muscle mass and attenuation were performed using Student's t-test. Cox regression analysis was used to examine the association between muscle mass and attenuation and all-cause readmissions. In multivariate Cox regression analysis, the covariates included age, sex, and EuroSCORE II. The Kaplan-Meier curve and log-rank test were performed to examine the im-

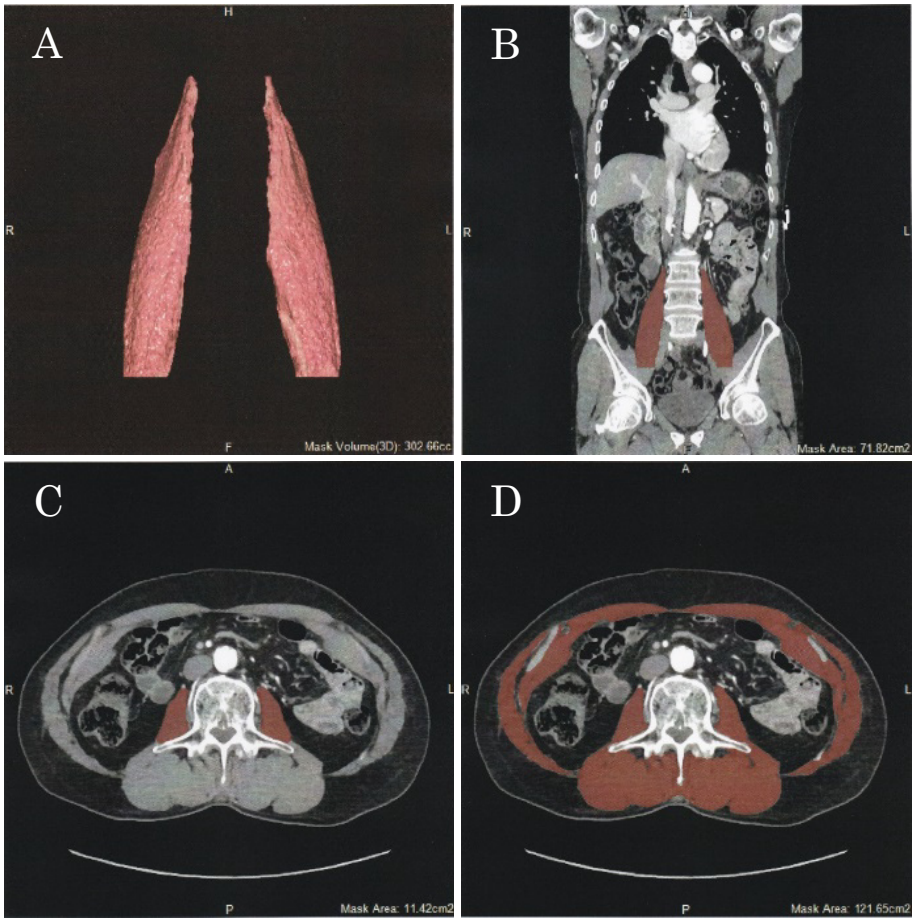

Fig. 1. Assessment of skeletal muscle in CT images.
Psoas muscle volume in the three dimensions (A) and in the coronal plane (B). Psoas muscle area (C) and total muscle (D) at the third lumbar vertebra in the axial plane.

pact of muscle quantity and quality on all-cause readmissions using stratified median PMV and MA. A p-value of less than 0.05 was considered significant. Statistical analyses were performed using SPSS 21.0 (IBM Corp., New York, USA).

Results

Baseline characteristics

Clinical characteristics at baseline are shown in Table 1. The mean age was 85 ± 5 years, and women accounted for 69% of all patients. In terms of New York Heart Association (NYHA) class, 15 patients were in class I, 63 patients were in class II, 32 patients were in class III, and three patients were in class IV. The median left ventricular ejection fraction was 61.7% (interquartile range: 56.4-65.0%) in all patients. EuroSCORE II, a risk score for cardiac surgery, was a median 3.4% (interquartile range: 2.1-5.2%) in all patients. Mean grip strength was 16.2 ± 6.7 kg, and mean gait speed was 0.75 ± 0.26 m/sec in all patients.

Muscle mass and attenuation of skeletal muscle

PMV, PMA, TMA, and their MA are shown in Table 2. The crude or normalized for height squared PMV, PMA, and TMA were significantly larger in men than in women (all $p < 0.001$). The MA of the PMV and TMA were significantly higher in men than in women ($p < 0.001$ and $p = 0.006$, respectively).

Endpoint and follow-up

The median follow-up period in all patients was 724 days (interquartile range: 528-730 days). There were 25 all-cause readmissions during the follow-up period (22% of all patients). There were 13 readmissions due to cardiac causes (52% of the all-cause total), and eight among cardiac causes were because of heart failure (32% of the all-cause total). There were 12 readmissions due to non-cardiac causes (48% of the all-cause); of these, fractures were most common (six events, 24% of the all-cause total).

Association of muscle mass and attenuation with all-cause readmission

The results of the Cox regression analysis for all-cause readmission are shown in Table 3. In the univariate analysis, PMV and MA were significant predictors of all-cause readmission, whereas the PMA and TMA and each of the

MA were not. In the multivariate analysis adjusted for age, sex, and EuroSCORE II, the PMV and its MA and crude PMA were significantly associated with all-cause readmission. Our findings demonstrated that PMV, MA, and crude PMA were inversely related to risk of all-cause readmission.

Table 1. Baseline characteristics

	Overall (n = 113)
Age (years)	85 ± 5
Women (%)	69
Height (cm)	150.2 ± 8.5
Body mass index (kg/m^2)	22.5 ± 3.3
NYHA class (I/II/III/IV) (%)	13/56/28/3
Comorbidity	
Hypertension (%)	72
Dyslipidemia (%)	48
Diabetes mellitus (%)	22
Previous myocardial infarction (%)	5
Previous angina pectoris (%)	19
Chronic obstructive pulmonary disease (%)	4
Previous stroke (%)	12
Previous motor disorder (%)	25
Transthoracic echocardiography	
Left ventricular ejection fraction (%)	61.7 (56.4-65.0)
Aortic valve area (cm^2)	0.7 ± 0.1
Mean pressure gradient (mmHg)	51.6 (42.1-62.3)
Laboratory data	
Albumin (g/dl)	3.9 ± 0.4
eGFR (ml/min/1.73 m^2)	52.8 (38.4-61.5)
Creatinine (mg/dl)	0.92 (0.73-1.11)
EuroSCORE II (%)	3.4 (2.1-5.2)
Physical function	
Grip strength (kg)	16.2 ± 6.7
Gait speed (m/sec)	0.75 ± 0.26

Values are mean ± standard deviation, percentages, or median (interquartile range). NYHA, New York Heart Association; eGFR, estimated glomerular filtration rate.

The Kaplan-Meier survival curves for all-cause readmission divided according to the normalized PMV and its MA are shown in Figure. 2. The median of the normalized PMV was 68.0 cm^3/m^2 for women and 96.3 cm^3/m^2 for men, and the median of the MA of the normalized PMV was 36.4 HU for women and 41.8 HU for men. In the results divided according to normalized PMV, the low PMV group had a significantly higher incidence of all-cause readmission than the high PMV group (log-rank test: p = 0.048) (Fig. 2A). The low MA group had a significantly higher incidence of all-cause readmission than the high MA group (log-rank test: p = 0.043) (Fig. 2B). The group with low PMV and MA had a significantly higher incidence of all-cause readmission than the group with high PMV and MA (log-rank test: p = 0.011) (Fig. 2C).

Discussion

This was the first report to show that loss of the PMV assessed by CT was an independent predictor of post-discharge all-cause readmission in patients who underwent TAVI. The novelty of this study was the evaluation of not only the psoas muscle mass, but also its MA. The risk of readmission after discharge was significantly greater in the group with both low values of the PMV and its MA than in the group with both high values. Assessing muscle quality in addition to muscle mass may more accurately predict all-cause readmission after TAVI.

It has been reported that the loss of muscle mass assessed using CT is associated with prognosis after TAVI. The decrease in the PMA at L3 or the fourth lumbar vertebra (L4) independently predicted 30-day and cumulative mortality rates after TAVI[18]; although this result showed

Table 2. Muscle mass and attenuation of Skeletal muscle in CT images

	Overall (n = 113)	Women (n = 78)	Men (n = 35)	p-value
Crude				
PMV (cm^3)	170.7 ± 59.9	141.1 ± 33.5	236.6 ± 52.8	< 0.001
PMA (cm^2)	9.4 ± 3.2	8.1 ± 2.3	12.3 ± 2.9	< 0.001
TMA (cm^2)	80.4 ± 24.0	71.0 ± 15.6	101.3 ± 26.4	< 0.001
Normalized for height squared				
PMV (cm^3/m^2)	74.4 ± 20.4	66.1 ± 15.1	93.0 ± 18.7	< 0.001
PMA (cm^2/m^2)	4.1 ± 1.2	3.8 ± 1.1	4.9 ± 1.2	< 0.001
TMA (cm^2/m^2)	36.1 ± 7.8	33.9 ± 6.8	41.2 ± 7.5	< 0.001
Muscle attenuation (HU)				
PMV	37.3 ± 5.6	36.0 ± 4.8	40.2 ± 6.0	< 0.001
PMA	35.9 ± 6.4	35.3 ± 6.0	37.3 ± 7.0	0.133
TMA	28.8 ± 8.5	27.4 ± 7.5	32.1 ± 9.8	0.006

Values are presented as mean ± standard deviation. PMV, psoas muscle volume; PMA, psoas muscle area; TMA, total muscle area; HU, Hounsfield unit.

Table 3. Association of muscle mass and attenuation with all-cause readmission

	Unadjusted		Adjusted for age/sex		Adjusted for age/sex/ EuroSCORE II	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Crude						
PMV	0.988 (0.980-0.997)	0.008	0.980 (0.968-0.992)	0.001	0.978 (0.965-0.991)	0.001
PMA	0.879 (0.764-1.012)	0.073	0.858 (0.719-1.024)	0.090	0.812 (0.667-0.988)	0.037
TMA	0.996 (0.980-1.012)	0.585	0.999 (0.979-1.021)	0.947	0.997 (0.976-1.020)	0.816
Normalized for height squared						
PMV	0.970 (0.949-0.992)	0.008	0.961 (0.936-0.988)	0.005	0.957 (0.930-0.985)	0.003
PMA	0.792 (0.556-1.129)	0.197	0.813 (0.549-1.205)	0.303	0.722 (0.472-1.105)	0.134
TMA	0.994 (0.942-1.049)	0.840	1.006 (0.947-1.069)	0.845	0.999 (0.937-1.065)	0.979
Muscle attenuation						
PMV	0.922 (0.864-0.985)	0.016	0.922 (0.859-0.989)	0.023	0.927 (0.862-0.997)	0.040
PMA	0.973 (0.916-1.034)	0.383	0.977 (0.918-1.041)	0.474	0.978 (0.916-1.044)	0.506
TMA	0.962 (0.924-1.001)	0.057	0.963 (0.923-1.004)	0.079	0.968 (0.925-1.012)	0.151

HR, hazard ratio; CI, confidence interval; PMV, psoas muscle volume; PMA, psoas muscle area; TMA, total muscle area.

different prognostic importance than our result, decreased muscle mass was associated with poor outcomes in a similar fashion to what we showed in this study. To the best of our knowledge, there are no studies examining the association between CT-assessed skeletal muscle mass and readmission in patients who underwent TAVI; however, there are several reports regarding other diseases[19,20]. Although the subjects and the survey period differed from those described above, the results of this study showed similar trends. Loss of PMV was an independent predictor of readmission after discharge in TAVI patients.

There are several reports on the association between PMA and all-cause mortality after discharge in patients who underwent TAVI; however the association remains controversial. In these patients, the PMA at L4 was a predictor of 12-month all-cause mortality in receiver operating characteristic analysis[21]. In contrast, the PMA at L3 was not associated with an increased risk of all-cause mortality at 1 year in patients who underwent TAVI[22]. It was reported that the PMA at the L3 or L4 was associated with all-cause mortality only in women[23,24] or only in men[25] in patients with TAVI.

In recent years, reports on the evaluation of the psoas muscle by CT images included evaluations of not only the cross-sectional area but also the volume. In patients with pancreatic cancer who underwent pancreatic resection, the PMV, and not the PMA, predicted postoperative complications and all-cause mortality[14]. In the present study, we showed that low PMV was an independent predictor of post-discharge readmission in TAVI patients.

It was speculated that more accurate evaluation of the psoas muscle was possible by using the volume rather than the cross-sectional area. Spinal deformity tends to become more pronounced with age[26,27]. Patients undergoing TAVI tend to be very old and often have substantial spinal deformities; it was speculated that the PMV was more suitable as a method for evaluating the muscle mass of the psoas muscle than the PMA. Several reports have revealed that frailty is an independent predictor of readmission after TAVI[28,29]. It was speculated that patients with reduced muscle mass may be more prone to the frailty cycle owing to reduced physical reserve and higher risk of readmission.

In the evaluation of skeletal muscle, the importance of evaluating not only muscle mass but also muscle quality has been drawing attention. In CT images, increasing lipid content in the skeletal muscle was associated with decreased MA[30]. In a report of volunteers aged 59-85 years, the MA of the TMA at the level of the second lumbar vertebra correlated with grip strength[16]. Lower MA of the TMA at L3 was an independent predictor of all-cause mortality, and both low MA and muscle mass were associated with increased risk of all-cause mortality in patients who underwent TAVI[31]. Similar to previous reports, in this study, the MA of the PMV independently predicted readmission after discharge, with both low MA and muscle mass indicating high risks of readmission. Low MA has been shown to be correlated with insulin resistance[32], increased inflammatory cytokine levels[33], and physical inactivity[34] all of which are associated with worse clinical outcome.

CT examinations are routinely performed preoperatively in TAVI patients. Muscle quantity and quality assessment are possible to grasp the risk of readmission and early referral to physical therapy. Early detection of muscle quantity and quality and early referral to physical therapy may reduce the risk of readmission.

This study has several limitations. First, this study was conducted at a single center, and the study design was retrospective. Second, the number of samples was relatively small. Multicenter prospective studies with large sample sizes are needed to test whether the findings of this study

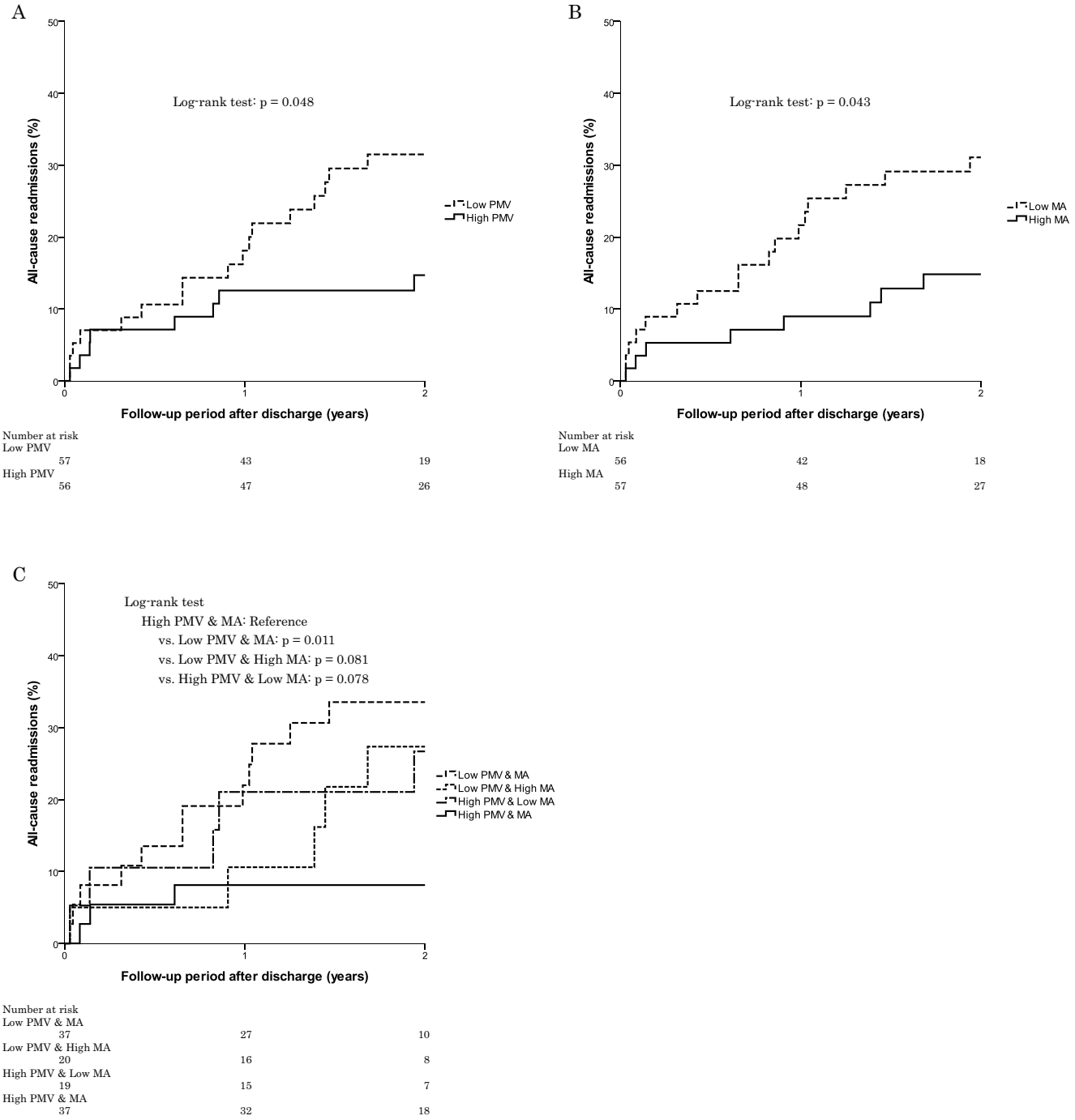

Fig. 2. Kaplan-Meier curves for all-cause readmission divided according to the normalized PMV and its MA for each sex. Divided according to PMV (A), its MA (B), and both PMV and its MA (C). PMV, psoas muscle volume; MA, muscle attenuation.

are widely applicable to patients undergoing TAVI. Third, skeletal muscle mass was only assessed in individual muscles by CT images and was not assessed in systemic muscle using dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis, both of which are standards for sarcopenia evaluation. It is unclear whether the PMV-decreased cases in this study caused systemic muscle loss; however, a previous study showed a high correlation between systemic muscle mass evaluated by DXA and cross-sectional area of muscle evaluated using CT images[9].

Conclusion

We showed that the PMV and its MA measured from preoperative CT images independently predicted post-discharge all-cause readmission in patients who underwent TAVI. In addition, both low PMV and its MA were associated with increased post-discharge readmissions. These findings suggest that accurate evaluations of muscle mass and quality are necessary to assess the risk of post-discharge readmissions in TAVI patients.

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Conflict of Interest: The authors have no conflict of interest to disclose.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Development and Comparative Efficacy of Lagos Neuropathy Protocol for Improving Recovery of Symptom and Functional Independence Performance in Individuals with Diabetic Peripheral Sensorimotor Polyneuropathy

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ABSTRACT. Background: Diabetic peripheral sensorimotor polyneuropathy (DPSP) has been treated with sketchy outcomes and available approaches are not applicable for self-administration. This study developed protocol for managing symptoms of DPSP and assessed its comparative efficacy. Methods: Study developed *Lagos Neuropathy Protocol (LNP)* through existing concept in DPSP and tested its safety, clinical applicability, and ease of self-administration. Its efficacy was compared with *Buerger-Allen Exercise* (*BAE*) by involving 31(11males) with DPSP, randomized into *LNP* and *BAE* and treated for 10-week. Toronto Clinical Scoring System was used to diagnose DPSP while Diabetic Neuropathy Examination was used to diagnose distal polyneuropathy. Sensory/pressure perception was assessed using 10 g-monofilament while Short Physical Performance Battery, Bergs Balance Scale and Visual Analogue Scale was used to assess functional performance, strength and balance, and pain respectively. Results: *LNP* has three domains: sensory/pressure/proprioception, strength/balance, and pain/swelling. Most (80%) of the participants rated the *LNP* as excellently safe while the rest (20%) rated as very good in safety. All the participants rated *LNP* excellent in terms of self-administration and suitability for clinical use without adverse effect. The mean age of the participants for the comparative phase was 66.20±9.48years while their length of diagnoses of diabetes was 15.80±13.35 years. About a third (32.5%) had DPSP. Both *LNP* and *BAE* had significant improvement ($p<0.05$) in sensory/pressure perception, pain, strength and balance, and functional performance but *LNP* had better significant improvement. Conclusion: *LNP* is safe, good for self-administration, clinically applicable and efficacious in improving sensory/pressure perception, balance, pain and functional performances in individuals with DPSP.

Key words: Protocol development, Pressure and sensory perceptions, Strength and balance, Functional performance, Diabetes peripheral sensorimotor polyneuropathy

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Despite the number of patients affected by diabetic peripheral sensorimotor neuropathic pain (DPSP), there is no available treatment protocol that addresses all its symptoms and improve functional performance in individuals living with it. In the pathology of DPSP, a number of metabolic and vascular changes interconnect to cause damage to nerve cells[1,2)]. Hence, it is only a thorough understanding of its clinical manifestations that will help appropriate and effective treatment[3)]. All types of nerve fibres, such as sensory,

autonomic, motor, both myelinated and unmyelinated, are adversely affected in people with diabetes[2]. This has resulted in the choices of multiple drug therapies including non-steroidal anti-inflammatory for its treatment[1]. However, none of it have yielded satisfactory outcomes in addition to their consequential side effects and complications. This has informed the use of other conventional approaches such as provision padded foot-wears, massage self-care education to reduce rates of ulceration and even amputation[3]. However the outcomes are not sustainable and has not met the needs of the patients.

The most feared complication of DPSP is diabetic foot, where the loss of protective sensation often accompanied by reduced perfusion from arterial disease increases the risk of ulceration, infection and, ultimately amputation[4]. However, at least half of the foot ulcers that occur in people with DPSP could be prevented by appropriate management[4]. It can interrupt the afferent and efferent functions of the lower extremities that are responsible for maintaining normal posture and normal walking and often results in loss of proprioception with inability to monitor the progression of any movement sequence resulting in clumsy gait[5-7]. Failure to diagnose and properly manage these symptoms of DPSP can lead to serious consequences, including disability and amputation[1]. However, the gap still remains the non-availability of appropriate and accessible treatment protocol. hence, there is need for an affordable, accessible and easily implemented protocol that is amenable to clinical practice in any setting to ameliorate the menace of DPSP and prevent the complications that may occur.

Although some approaches such as range of joint motion, stretching exercises and proprioception and balance exercises have been suggested as conservative methods in the management of DPSP[1,3,8], none of it has been able to address the symptoms still allowing the condition to progress to irreversible complications. Despite the fact that a monochromatic near-infrared has produced better improvement in sensation and balance, and reduce pain in the feet of individuals DSPS[1], the approach remains only of research importance as it is not easily affordable and cannot be use without supervision which has made both clinical and home use much impracticable. Most importantly, it is does not address muscle weakness and proprioception which are important causes of disability in individuals with DPSP.

Although, more recently, the *Buerger-Allen Exercise* (*BAE)* have been favoured in the management of diabetes neuropathy[9-11]. However, none of the aforementioned approaches including the *BAE* has produced the desired results and patients have been left to live with the sequels and the complications of DPSP. Although *BAE* and proprioception with balance exercise are good for patients with DPSP in the aspect of increasing lower extremity perfusion, speeding up wound healing, increasing sole and plantar perception and helps to improve balance and postural control[9-11], limited carryover effect of the treatments have been reported which has eroded its clinical importance. It has also fall short in addressing all other important symptoms and sequels of DSP especially pain, sensory and pressure perception, muscle weakness and most importantly the consequential functional limitation. It is therefore pertinent to develop a clinically applicable approach/protocol that will effectively address all the symptoms of DPSP and prevent disability. For this to be effective, a patient must be able to apply it outside the clinical setting without any difficulty or anticipated adverse effect. This will help in both the prevention and effective management of DPSP and avoid inherent complications. Therefore, this study developed a safe, clinically applicable, home-use friendly and clinically effective approach for the management of symptom of DPSP and improving functional independence performance in individuals with DPSP. It also determined the concurrent efficacy the approach using a preferred existing treatment approach for DPSP.

Methods

The protocol for this research was approved by the Health Research Ethics Committee of The Lagos University Teaching Hospital, Lagos Nigeria approved this study (ADM/DCST/HREC/APP/1534). All participants consented for their participation in this study. There is also no conflict of interest either from the authors or the participants for this study. This study was conducted in two phases. The first phase involved the development of the *LNP* while the second phase involved and testing for safety, efficacy, adverse effect, appropriateness for self-administration and the comparative efficacy test using the *BAE* as the gold standard. The development phase involved the development of the content of the protocol using search engines: Hinari, PubMed and Google Scholars with specific search words: Diabetes, diabetes symptoms, diabetes peripheral neuropathy, diabetes sensorimotor neuropathy, diabetes neuropathy, diabetes disability, functional limitation in diabetes, treatment of diabetes neuropathy, and outcomes of approaches for treatment of diabetes neuropathy. The choice of the words was based on the existing concept of diabetes sensorimotor peripheral polyneuropathy. At the end of the search, the following themes were generated: sensory deficit, pressure deficit, pain, proprioceptive deficit, exercises therapy, balance deficiency, peripheral neuropathy, diabetes, function limitation, muscle weakness and anti-inflammatory drug. These was further synthesized with the following themes finally arrived at: sensory deficit, proprioception, balance deficit, muscle weakness, functional limitation and pain. Hence, the approach was further elucidated by inputting these final words into the search engines with addition of management to each of the words. The outcomes of the search were aggregated to form a 10-station

Table 1. Lagos Neuropathy Protocol

Station	Equipment/Instrument	Activities performed	Purpose/Goals
1	10cm by 10cm-by-10cm foam	Walks on foam and drag feet on it for 5 minutes	Improve sensation and proprioception
2	10cm by 10cm by 10cm wooden box half-filled with dry grains/ corns/beans seeds	Matches and squeezing feet on seeds for 5 minutes	Improve sensation and proprioception
3	4cm by 4cm by 4cm moderate density mat	Walks and drags feet on mat it for 5 minutes	Improve sensation and proprioception
4	10cm by 10cm by 10cm wooden half- cotton wool	Walks and drags feet on cotton-wool for 5 minutes	Improve sensation and proprioception
5	Blunted/rough surfaced 10cm by 10cm by 10cm mat with contours	Walks and drags feet on mat it for 5 minutes	Improve sensation and proprioception
6	Proprioceptive ball, 8cm diameter	Stands and bounces on it	Improve proprioception
7	Elastic exercise band to train and strengthen the ankle	Train and strengthen ankle using hold-relax approach	Improve strength
8	Wobble board to train balance in standing	Train balance in standing for 5 minutes	Improve balance
9	Therapy ball, 75cm in diameter	Train balance and hip movement	Improve balance
10	Contrast bath	To treat pain and improve sensory perception. Deep feet in bowl that contains 75% ice and 25% water that covers above the ankle at temperature <5°C for 5 minutes. Remove the feet and deep it in another bowl of water at between 28°C and 35°C for 5 minutes. Repeat the cycle 3 times. After this a gentle effleurage massage is performed on the foot in elevation.	To treat the pain, improve sensory perception and drain swelling

protocol addressing proprioceptive, muscle strengthening and balance training, sensory and pressure perception training. These were aggregated into three domains: sensory/pressure/proprioception, strength/balance, and pain/swelling to form the *LNP*. Stations one to six were for proprioceptive training, station seven for strengthening, stations eight and nine were for balance training and station is for relieving pain, improving sensory perception and drain swelling (table 1).

For effectiveness, a patient must follow the order of the treatment starting from station one and ending at station ten. Safety, clinical applicability, ease of home-use, adverse effect was assessed using proforma and self-diary. This process was conducted for 10 weeks.

For the second phase, 163 individuals clinically diagnosed of diabetes mellitus and attending endocrinology/diabetes clinic of a teaching hospital were screened for diabetic peripheral sensorimotor polyneuropathy (DPSP). The presence and severity of DPSP was determined with the use of Toronto Clinical Scoring System (TCSS) while distal polyneuropathy was diagnosed with Diabetic Neuropathy Examination Scoring System (DNE). The maximum score on DNE is 16 points and a score of greater than three points is considered abnormal[12]. The maximum score on TCSS is 19 points[13,14] with scores zero to five being classified as having no DPSP, 6 to 8 as mild DPSP, 8 to 11 as moderate DPSP; and 12 to 19 as severe DPSP[13,14]. Participants were included if they had $\geq$3 on DNE and $\geq$6 on TCSS. Those with gangrenous foot, diabetes foot ulcer, diabetes amyotrophy or amputation were excluded from this study. Out of the 163 individuals screened, 53 of them met the criteria for the diagnosis of DPSP while 31 out of the 53 who consented to participated in the study. They were randomized into *LNP* and a control using the *BAE* protocol. They participated in the 10 weeks interventional programme for *LNP* and *BAE* treatments. The *BAE* exercise group served as a gold standard for the *LNP* intervention group. Sensory perception was assessed using Semmen-Weistein© 10 g monofilament while the Short Physical Performance Battery (SPPB), Bergs Balance (BBS) and Visual Analogue Scale (VAS) was used to assess functional independence, balance performance and pain respectively. The SPPB is a group of measures that combines the results of the gait speed, chair stand and balance tests with scores range from 0 (worst performance) to 12 (best performance)[15]. The Berg Balance Scale (BBS) was used to evaluate the subject's balance performance. The scores ranged from zero to 56 with 41 to 56 indicating low fall risk, 21 to 40 depicting medium fall risk and 0 to 20 being classified as high fall risk[16]. The VAS is a validated, subjective measure for acute and chronic pain. Scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between "no pain" and "worst pain"[17]. Participants received no other treatment for DPSP apart from the treatment of the group they were assigned to and their normal consultation with their Physicians and Dieticians. The proprioception with balance exercises consists of ten stations with various tasks to stimulate the sole of the feet and balance training exer-

Table 2. Demographic Profile of the Participants at Baseline

Variables	Lagos Neuropathy Protocol (n=15) Mean±SD	Buerger-Allen Exercises (n=16) Mean±SD	t-values	p-values
Age (Years)	66.20±9.48	60.43±13.26	1.398	0.173
Height (m)	1.63±0.05	1.69±0.09	-2.65	0.014*
Weight (Kg)	75.0±17.56	79.76±17.26	-0.76	0.454
Body Mass Index (Kg/m^2)	23.3±1.34	21.87±1.108	0.328	0.745
Length of Diagnoses of Diabetes Mellitus (Years)	15.80±13.35	10.25±4.90	1.517	1.47

$p<0.05$

*Significant different exists

cises. The control group performed *BAE*. It involved the individual lying flat in bed with the legs elevated at 45 degrees until blanching occurs or for a maximum of 2 minutes, then sitting in high sitting to perform ankle dorsiflexion, plantarflexion, eversion, inversion, flexion and extension of the toes for a minimum of 2 minutes or until rubor appeared[11]. Finally, the participant lies supine with the feet covered with a warm blanket for 5 minutes. The whole cycle was repeated 3 to 6 times each session[9]. The participants in both groups performed the protocols three times per week at a minimum of a day interval in the clinic and at home for the days they were not in the clinic (i.e. the day before coming to the clinic) for the 10 weeks. Their compliance and performance at home was assessed the next day they appeared at the clinic through meticulous interview for process and procedure. Both group of participants continued their consultation with their Physicians for their glycemic control but none of them was prescribed any analgesic. Even those who were previously on analgesic were withdrawn from them with a placebo prescribed instead especially those who do not want to be taken out of their analgesics to give them a sense of use. We were in contact with the Physicians throughout the course of the study to be sure that all the participants had adequate glycemic control.

Data Analysis

Data was analyzed using the Statistical Package for Social Sciences (SPSS version 22) and was summarized using descriptive statistics of frequency, mean, and standard deviation. Compliance and comments of the participants to *LNP* were analyzed using thematic analysis safety, friendliness, adverse effect, ease of application and clinical benefits. The second phase was analyzed using independent and paired t-tests, Mann-Whithney-U and Wilcoxon sign rank tests. Data was analyzed using the mean difference of scores in each of the groups with intention to treat analysis ($p<0.05$).

Results

In the first phase of the study, a 10-station exercises and treatment were developed for the management of symptoms of DPSP and for improving functional performance in individuals with DPSP. Out of the 163 individuals with diabetes mellitus screened for DPSP in phase two, 53 had DPSP giving a prevalence rate of 32.5%. Eleven (35.5%) out of the 31 participants were males while 20 (64.5%) were females. Out of the 15 participants in *LNP*, 4 (26.7%) were male while 11(73.3%) were females while out of the 16 participants in *BAE*, 7(43.8%) were male while 9(56.3) were females. Most 22(71%) of the participants were married, 8(25.8%) were widowed while only one was yet to be married. Twelve (38.7%) participants each had secondary and post-secondary education while 7 (22.6%) had primary education. The participants were aged 66.20± 9.48 years and had been diagnosed of diabetes mellitus for 15.80±13.35 years. Their weight, height, and body mass index were 75.01±17.56 Kg, 1.63±0.05 m and 23.3± 1.34 Kg/m^2 respectively. The two groups did not significantly differ ($p>0.05$) in age, year of diagnoses of diabetes mellitus, weight and body mass index except in height with *BAE* having significantly ($p=0.014$) taller (table 2). There was rapid numerical reduction in the neuropathic symptoms and body mass index in the two groups but there was more rapid numerical normalization in the *LNP* group (table 3). The two groups of participants were matched at baseline in all neuropathic symptoms as well as in balance performance except in functional performance where the *BAE* were significantly more functional in both functional chairs standing ($p=0.018$) and in overall function ($p=0.030$) (table 4). The *LNP* ratings for safety, adverse effect, ease of home-use and clinical application, 12(80%) rated *LNP* excellent for safety while 3(20%) rated it as very good. All of them (100%) rated it excellent for ease of application at home and also for clinical application while no one reported any adverse effect. Both groups improved significantly ($p<0.05$) in their neuropathic symptoms scores, sensory and pressure perception score, balance performance and functional performance after the interventions (tables 5

Table 3. Clinical Symptoms and Anthropometric Characteristics of the Participants

Variables	All Participants		Lagos Neuropathy Protocol		Buerger-Allen Exercises	
	Pre-Int	Post-Int	Pre-Int	Post-Int	Pre-Int	Post-Int
	n	n	n	n	n	n
Fall Risk						
No risk of fall	0	18	0	12	0	6
Low fall risk	3	9	1	3	2	6
Medium fall risk	6	4	2	0	4	2
High fall risk	22	0	12	0	10	0
Diabetic peripheral sensorimotor polyneuropathy						
None	0	0	6	0	0	0
Mild	0	14	0	7	0	7
Moderate	6	11	2	2	2	9
Severe	25	0	13	0	12	0
Body Mass Index (Kg/m^2)						
Normal weight (18.5-24.9)	11	20	5	12	6	8
Overweight (25-29.9)	11	8	7	3	4	5
Obesity Class 1 (30-34.9)	4	3	1	0	3	3
Obesity Class 2 (35-39.9)	3	0	1	0	2	0
Extreme Obesity Class 3 (>40)	2	0	1	0	1	0
Sensory and Pressure Perception						
Present	7	22	2	15	5	7
Absent	24	9	13	0	11	9
Pain						
Present	17	5	9	0	8	5
Absent	14	22	6	15	11	9
Swelling						
Present	15	5	9	0	6	5
Absent	14	22	6	15	11	9

LNP = Lagos Neuropathy Protocol

BAE = Buerger-Allen Exercises

and 6) as well as in pain ($p<0.05$). The proprioceptive and strengthening with balance exercise group performed significantly better ($p<0.05$) in sensory and pressure perception score, functional performance (balance test domain, gait speed domain and chair stand test domain) and balance performance after the interventions (table 7) and in pain.

Discussion

The main aim of this study was to develop a safe, clinically applicable, self-care home-use friendly and clinically effective protocol for the management of symptoms of DPSP and for improving functional independence performance in individuals with DPSP. It also determined the comparative efficacy of the protocol using an existing treatment approach for DPSP. This study has developed a protocol, Lagos Neuropathy Protocol (*LNP*) that is safe, has ease of home-use, clinically applicable and efficacious in improving sensory and pressure perception, balance performance, pain and functional independent performances in individuals with diabetic peripheral sensorimotor polyneuropathy. This is of clinical significance as this protocol has been able to address all the symptoms of diabetes peripheral sensorimotor neuropathy effectively. Hence, with this protocol, little or no disability related to diabetes sensorimotor polyneuropathy will occur. Another important aspect of this protocol is that it can be easily be self-administered without supervision. This protocol can also be useful for the prevention of neuropathy in diabetes or other related endocrinology or neurological disorders.

It is also of clinical importance that the *Lagos Neuropathy Protocol* is more efficacious than *Buerger-Allen Exercises* in improving sensory, balance, pain and functional performances in individuals with diabetic peripheral sensorimotor polyneuropathy. Although with *Buerger-Allen Exercises* and proprioception and balance exercises are two of the preferred treatment of choice to avoid or limit predisposition to a diabetic foot ulcer[8], they have not been able to address some of the principal complications of diabetes peripheral sensorimotor neuropathy especially in the aspects

Table 4. Comparison of Clinical Variables Between the two Groups Before the Interventions

Variables	Group	n	Mean Rank	Sum of Rank	U-value	Z-value	p-value
Diabetic Neuropathy Examination Score	LNP	15	15.17	227.5	113.25	-0.277	0.788
	BAE	16	16.78	268.5			
Diabetic Peripheral Neuropathy Symptoms Score	LNP	15	19.47	292	85	-1.469	0.243
	BAE	16	12.75	204			
Diabetic Peripheral Neuropathy Sensory Score	LNP	15	15.7	235.5	113.25	-0.286	0.776
	BAE	16	16.28	260.5			
Total Diabetic Peripheral Neuropathy score	LNP	15	17.12		103.25	-0.692	0.513
	BAE	16	14.96				
Sensory perception test score	LNP	15	18.32	256.5	72.5	-1.692	0.91
	BAE	16	13.03	208.5			
Functional balance test score	LNP	15	13.83	207.5	87.5	-1.488	0.137
	BAE	16	18.03	288.5			
Functional Gait speed test score	LNP	15	14.33	215	95	-1.212	0.226
	BAE	16	17.56	281			
Functional Chair Stand test score	LNP	15	12.33	185	65	-2.358	0.018
	BAE	16	19.44	311			
Total Functional performance test score	LNP	15	12.37	185.5	65.5	-2.211	0.03
	BAE	16	19.41	310.5			
Balance Performance Score	LNP	15	14.63	219.5	99.5	-0.977	0.423
	BAE	16	17.28	276.5			

$p<0.05$
LNP = Lagos Neuropathy Protocol
BAE = Buerger-Allen Exercises
n = number of participants

of pain, sensory and pressure perception and functional performances. This *Lagos Neuropathy Protocol* has been able to provide the needed anti-dote to these complications. Hence, this *Lagos Neuropathy Protocol* has made available more evidence-based approach in managing diabetes peripheral sensorimotor polyneuropathy.

The fact that approximately one-third of the population assessed had peripheral neuropathy shows the clinical significance of diabetes peripheral sensorimotor polyneuropathy as a usual complication of diabetes mellitus. It bestowed on clinicians to develop a strategy at preventing its occurrence and effectively manage it when it occurs. Fortunately, the availability of *the LNP* has now made it easier to manage the symptoms of DPSP and prevent complication. This prevalence agrees with those of Agrawal *et al*[18] and Kluding *et al*[19] that diabetes neuropathy is the common complication of diabetes and is present in approximately one-third of people with diabetes aged 40 or older. On the same vein, Resnick *et al*[20] have earlier concluded that 30-40% of diabetic patients will show symptoms of diabetes peripheral sensorimotor polyneuropathy and the prevalence increasing with increasing in age, reaching approximately 44% among diabetic patients over 70 years. The prevalence finding in this study is very important as there is dearth of literature on the prevalence of diabetes peripheral sensorimotor neuropathy in this part of the world. The appropriate application of *LNP* will not only make the treatment of DPSP available, it will make it possible to stem down the prevailing complication.

The findings that both *LNP and BAE* were effective in improving neuropathic symptoms, sensory and pressure perception, in patients with diabetic peripheral neuropathy show that physiotherapy approaches are effective in the management of diabetes neuropathy and will prevent the dependency on multiple drugs therapy that may complicate their problems with other drug-induced side effects. However, the fact that the participants in the *LNP* had significantly better amelioration of neuropathic symptoms shows that *LNP* should be a preferred approach and treatment of choice in managing diabetes neuropathy. The result that participants in the *LNP* had a significantly better increase pressure perception on the foot and resulted in greater reduction in the number of insensitive points on the foot as compared with the *BAE* may be due to more increased stimulation of the foot proprioceptors and mechanoreceptors. Without prejudice to the fact that the glycemic control index of the participants in this study was not measure as indicator of outcome of intervention and the fact that the personal physical activities of the participants was not considered in the factor analysis which may be of limited effect

Table 5. Comparison of Outcome Variables Scores Within the Lagos Neuropathy Protocol Groups Before and After the Interventions

Variables	Group	Mean Rank	Sum of Rank	Z-value	p-value
Diabetic Neuropathy Examination Score	Negative Ranks	8	120	-3.453	0.001
	Positive Ranks	0	0		
Diabetic Peripheral Neuropathy Symptoms Score	Negative Rank	8	120	-3.462	0.001
	Positive Ranks	0	0		
Diabetic Peripheral Neuropathy Sensory Score	Negative Rank	8	120	-3.482	<0.001
	Positive Ranks	0	0		
Total Diabetic Peripheral Neuropathy score	Negative Rank	8	120	-3.425	0.001
	Positive Ranks	0	0		
Sensory perception test score	Negative Rank	8	120	-3.455	0.001
	Positive Ranks	0	0		
Functional balance test score	Negative Ranks	0	0	-3.542	<0.001
	Positive Ranks	8	120		
Functional Gait speed test score	Negative Ranks	0	0	-3.508	<0.001
	Positive Ranks	8	120		
Functional Chair Stand test score	Negative Ranks	0	0	-3.69	<0.001
	Positive Ranks	8	120		
Total Functional performance test score	Negative Ranks	0	0	-3.482	<0.001
	Positive Ranks	8	120		
Balance Performance Score	Negative Ranks	0	0	-3.464	0.001
	Positive Ranks	6.5	78		

$p<0.05$

Table 6. Comparison of Outcome Variables Scores Within the Buerger-Allen Exercises Group Before and After the Interventions

Variables	Group	Mean Rank	Sum of Rank	Z-value	p-value
Diabetic Neuropathy Examination Score	Negative Ranks	8.5	136	-3.564	<0.001
	Positive Ranks	0	0		
Diabetic Peripheral Neuropathy Symptoms Score	Negative Rank	8	120	-3.464	0.001
	Positive Ranks	0	0		
Diabetic Peripheral Neuropathy Sensory Score	Negative Rank	8	120	-3.493	<0.001
	Positive Ranks	0	0		
Total Diabetic Peripheral Neuropathy score	Negative Rank	8.5	136	-3.573	<0.001
	Positive Ranks	0	0		
Sensory perception test score	Negative Rank	7	91	-3.256	0.001
	Positive Ranks	0	0		
Functional balance test score	Negative Ranks	0	0	-3.557	<0.001
	Positive Ranks	7.5	105		
Functional Gait speed test score	Negative Ranks	0	0	-3.64	<0.001
	Positive Ranks	8	120		
Functional Chair Stand test score	Negative Ranks	0	0	-3.535	<0.001
	Positive Ranks	8.5	136		
Total Functional performance test score	Negative Ranks	0	0	-3.44	0.001
	Positive Ranks	8	120		
Balance Performance Score	Negative Ranks	0	0	-3.162	0.002
	Positive Ranks	5.5	55		

$p<0.05$

Table 7. Comparison of Clinical Variables Between the two Groups After the Interventions

Variables	Group	n	Mean Rank	Sum of Rank	U-value	Z-value	p-value
Diabetic Neuropathy Examination Score	LNP	15	14.27	214	94	-1.085	0.318
	BAE	16	17.63	282			
Diabetic Peripheral Neuropathy Symptoms Score	LNP	15	15.37	230.5	110.5	-0.446	0.711
	BAE	16	16.59	265.5			
Diabetic Peripheral Neuropathy Sensory Score	LNP	15	14.13	212	92	-1.261	0.281
	BAE	16	17.75	284			
Total Diabetic Peripheral Neuropathy score	LNP	15	13.97	209.5	89.5	-1.252	0.232
	BAE	16	17.91	286.5			
Sensory perception test score	LNP	15	19.03	308.5	69.5	-2.192	0.04
	BAE	16	12.32	156.5			
Functional balance test score	LNP	15	19.53	398.5	67.5	-2.188	0.047
	BAE	16	13.83	197.5			
Functional Gait speed test score	LNP	15	19.59	341	65	-3.212	0.021
	BAE	16	12.32	185			
Functional Chair Stand test score	LNP	15	19.48	344	64	-3.338	0.011
	BAE	16	12.12	184			
Total Functional performance test score	LNP	15	19.28	308.5	67.5	-2.483	0.037
	BAE	16	12.5	187.5			
Balance Performance Score	LNP	15	14.12	376.5	69.5	-2.126	0.042
	BAE	16	19.44	219.5			

$p<0.05$
LNP = Lagos Neuropathy Protocol
BAE = Buerger-Allen Exercises
n = number of participants

because the participants in the two groups were matched for all indicators and they were reported by their Physicians to be within adequate glycemic control, this finding corroborates that of Kluding *et al*[19] who had earlier described improvements in outcomes related to neuropathic symptoms, cutaneous nerve fiber branching and measures of peripheral nerve function, glycemic control (HbA1c), and resting heart rate following supervised exercise in people with diabetic peripheral neuropathy.

The results of this study that *LNP* produced significant reduction in neuropathic symptoms supports the feasibility of exercise and physical agent's intervention in people with DPSP. The significant reduction in pain did not only lay credence to the effectiveness of *LNP* in managing pain in diabetes peripheral sensorimotor polyneuropathy, it has negated the previous controversies on whether exercise could effectively reduce pain or neuropathic symptoms[19]. This result agrees with Amaral *et al*[21] who had earlier observed good improvement of tactile sensitivity and the reduction of anteroposterior oscillations among diabetic women with peripheral neuropathy after proprioceptive training protocol and attributed the improvement to the multisensory nature of the stimulation provided by the intervention. Therefore, clinicians should integrate treatment protocol that consist of proprioceptive training exercises which may retard the progressive foot damage caused by diabetes peripheral sensorimotor polyneuropathy thereby decreasing their neuropathic symptoms and enhance better sensory perception.

Although larger sample size may be needed in further confirming the efficacy of *LNP* in reding disability in individuals with DPSP, the outcome of this study depicted that *LNP* is more effective than *BAE* in improving functional performance of patients with DPSP. The difference could be due to the incorporation of balance training in *LNP* which gives it more advantage over the *BAE* that concentrates on the foot movement alone. Although previous studies have documented the effectiveness of *BAE* on wound healing process among diabetic patients with foot ulcer[11] and greater improvement in vascular remodeling in the form of increased posterior tibial artery diameter, increasing walking distance and decreasing energy cost for walking (improving walking economy) in diabetic atherosclerotic patients suffering from intermittent claudication[22], there is dearth of literature on the effectiveness of *BAE* with respect to sensory and pressure perception and functional performance in individuals with diabetes neuropathy. Further study may be needed to explore the efficacy of *LNP* on foot ulcer and other complications of DPSP.

The fact that most of the participants did not have pain and a good number of them did not have swelling despite

the fact that greater percentage of them had loss their perception of sensory and pressure stimuli shows that diabetes neuropathy may not be accompanied with pain or swelling. Therefore, individual with diabetes should be routinely screened to detect early onset of neuropathy for adequate prevention and prompt treatment to avoid complication. Although this study did not set to find the effectiveness of *LNP* on weight control, it is interesting to see that most of the participants on the *LNP* had their weight being normalized despite some of them were overweight/obese before the intervention. Hence, the effectiveness of this *LNP* on weight control needs further investigation especially due to the fact that overweight and obesity is a common issue with people with diabetes mellitus.

Conclusion

Lagos Neuropathy Protocol is safe, has ease of self-administration, it is clinically applicable and efficacious in improving sensory and pressure perception, balance performance, pain and functional performances in individuals with diabetic peripheral sensorimotor polyneuropathy and it is more efficacious than *Buerger-Allen Exercises*.

Conflict of Interest: There is no conflict of interest.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Monophasic Pulsed Current Stimulation of Duty Cycle 10% Promotes Differentiation of Human Dermal Fibroblasts into Myofibroblasts

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ABSTRACT. Objective: Many clinical trials have shown the therapeutic effects of electrical stimulation (ES) in various conditions. Our previous studies showed that ES (200 μA and 2 Hz) promotes migration and proliferation of human dermal fibroblasts (HDFs). However, the effective duty cycle and the effect of ES on myofibroblast differentiation are unclear. This study aimed to investigate the relationship between duty cycle and myofibroblast differentiation. Methods: HDFs were subjected to ES (200 μA and 2 Hz) for 24 h with the duty cycle adapted at 0% (control), 10%, 50%, or 90%. α-smooth muscle actin (SMA) and transforming growth factor (TGF)-β1 mRNA and α-SMA protein expressions were assessed. Collagen gel contraction was observed for 48 h after ES initiation and the gel area was measured. Cell viability and pH of culture medium were analyzed for cytotoxicity of the ES. Results: Cell viabilities were decreased in the 50% and the 90% groups but ES did not influence on pH of culture media. ES with a duty cycle of 10% significantly promoted the mRNA expression of α-SMA and TGF-β1. α-SMA protein expression in the 10% group was also significantly higher than that of the control group. Collagen gel subjected to ES with a duty cycle of 10% was contracted. Conclusion: Duty cycle can influence on myofibroblast differentiation and ES with a duty cycle 10% is the effective for wound healing.

Key words: Electrotherpy, Pressure ulcer, Microcurrent, Wound healing

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Pressure injury is a chronic wound that decreases the quality of life of patients because of the associated pain and treatment costs[1)]. Thus, there is a need for an effective and low-cost treatment for pressure injury. Electrical stimulation (ES) treatment is recommended for pressure injury healing[2)], and clinical studies have shown its therapeutic effects against pressure injuries[3-6)]. Healing of chronic wounds is delayed because their inflammation period is prolonged and granulation tissue formation is inhibited[7)]. Granulation tissue formation is crucial for wound closure, and human dermal fibroblasts (HDFs) are a key factor in this process because their migration toward wound sites, proliferation, and differentiation into myofibroblasts are necessary for granulation tissue formation[8)]. Our previous studies showed that a monophasic-pulsed current (intensity; 200 μA, frequency; 2 Hz) promotes the migration of HDFs toward the cathode and their proliferation[9,10)], and that ES with the same conditions has a good therapeutic effect on pressure injuries[11)]. Thus, we revealed the optimum intensity and frequency of ES for pressure injury healing.

Myofibroblasts have a strong contractile ability and are involved in the wound healing process; the differentia-

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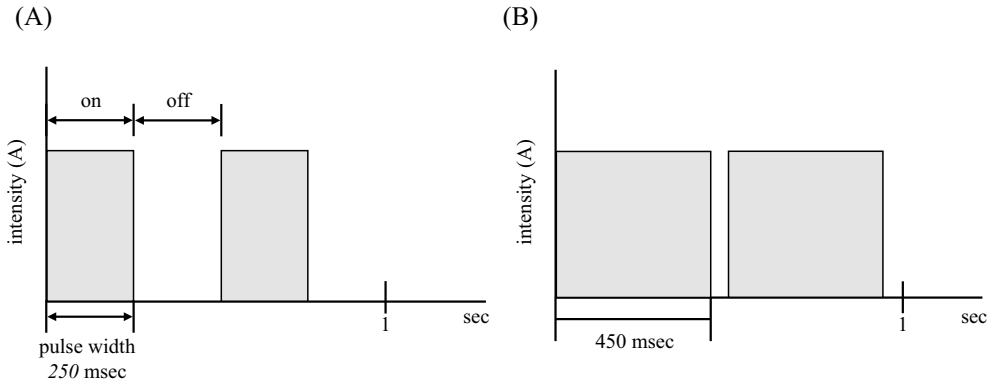

Fig. 1 Duty cycle.
Duty cycle is the on-off ratio of stimulation. Both figures present a 2-Hz monophasic pulsed current. Pulse width indicates stimulation duration during one stimulation cycle, and this is determined by the duty cycle and frequency. (A) The waveform with a duty cycle of 50% for which the on-off cycle is 1:1 and pulse width is 250 ms. (B) Duty cycle of 90%, with an on-off cycle of 9:1 and pulse width of 450 ms. The waveform approaches direct current as the duty cycle reaches 100%.

tion from fibroblasts to myofibroblasts results in granulation tissue contraction leading to wound closure[8]. Myofibroblasts are characterized by the expression of α-smooth muscle actin (α-SMA), and transforming growth factor-β (TGF-β) influences myofibroblasts to promote collagen synthesis in granulation tissue[12]. The effects of ES on the differentiation of HDFs have been demonstrated in *in vivo* and *in vitro* studies[13,14]. Direct current upregulates TGF-β1 and collagen I/III expression in mouse fibroblasts and promotes α-SMA expression in HDFs[13]. However, a pulse width of 300 ms within 600 ms promotes higher α-SMA expression in HDFs than a pulse width of 10 ms within 1200 ms[14]. Thus, the effects of ES on HDFs are influenced by pulse width. The pulse width is a result of the duty cycle, which is the on-and-off ratio of one stimulation (Fig. 1); a duty cycle of 100% indicates direct current, and the effect of duty cycle on HDF differentiation with an ES of 200 μA and 2 Hz, which promotes migration and proliferation in HDFs, is unclear.

Moreover, safety is mandatory for medical instruments including the ES device. In our previous studies, we did not assess the effects of long-term stimulation in HDFs. Low-intensity or small-electric fields within 10 h showed good effects on HDFs, promoting migration and proliferation[9,10,15,16]. Zhang et al. and Wang et al. showed that longer ES has good effects on the migration and secretion of pro-healing cytokines[14,15]; however, the therapeutic effects and adverse effects of long-term micro current stimulation in HDFs are not clear. Therefore, in this study, we adopted > 10-h stimulation and confirmed the effects of ES on cell viability. In clinical trials, it is necessary to decide the pulse width, as well as waveform, intensity, and frequency, to conduct ES. Thus, we hypothesized that the duty cycle might have an effect on promoting α-SMA expression in HDFs and their differentiation into myofibroblasts.

Method

Cell culture and electrical stimulation

Primary HDFs (CC-2511; Clonetics, San Diego, CA, USA) derived from a 33-year-old woman were used. HDFs were cultured in low-glucose Dulbecco's modified eagle medium (DMEM; Wako, Osaka, Japan) supplemented with 10% fetal bovine serum (Nichirei, Tokyo, Japan) and 5% penicillin-streptomycin Solution (Wako) in a CO_2 incubator at 37°C. HDFs that had undergone 3-7 passages were used in the experiments. HDFs were seeded in a 35-mm tissue culture dish (Wako) and cultured for 24 h. The culture medium was refreshed and platinum electrodes were set on both sides of a dish (Fig. 2). Thereafter, HDFs were subjected to monophasic-pulsed current stimulation (intensity, 200 μA; frequency, 2 Hz) for 24 h in a CO_2 incubator. HDFs without ES were used as controls. Duty cycles of 10%, 50%, or 90% were adapted to confirm the influence of differences in duty cycles.

Cell viability and cell number

The effect of ES on cytotoxicity was assessed because the ES that induces cell death cannot be clinically applied even if it promotes pro-fibrotic factors and the contractile ability of HDFs. Cell viability and cell numbers were analyzed after ES by trypan blue staining[17,18]. ES that induced cell death was not used to analyze gene and protein expression.

TaqMan real-time RT-PCR

To detect whether ES promoted fibroblast differentiation into myofibroblasts, the mRNA expression of α-*SMA* and *TGF-β1* were analyzed. After ES, the total RNA was extracted from HDFs using the High Pure RNA Isolation Kit (Roche, Basel, Switzerland). RNA was reverse-

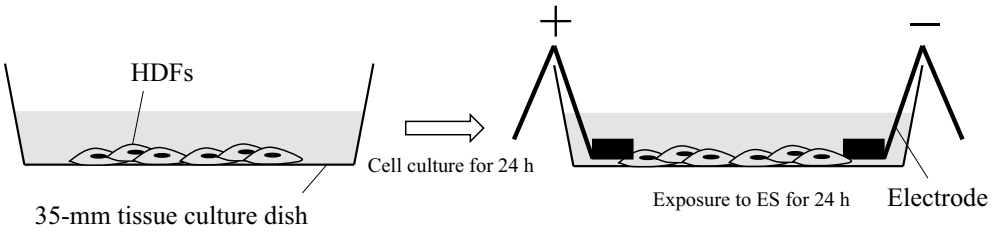

Fig. 2 Electrical stimulation.
Human dermal fibroblasts (HDFs) were seeded in a 35-mm tissue culture dish and cultured for 24 h in a CO_2 incubator at 37°C. Electrodes were set on both sides of a dish and connected to the electrical stimulation (ES) device. Then, HDFs were exposed to the ES for 24 h in a CO_2 incubator at 37°C.

transcribed into cDNA. The mRNA expression of α-*SMA*, *TGF*-β*1*, and *GAPDH* was then analyzed by TaqMan real time RT-PCR. Relative gene expression was calculated using the ΔΔCt method after normalization to *GAPDH* expression.

Western blotting

The expression of α-SMA is an indicator of myofibroblasts, and the expression of α-SMA was assessed by western blotting. After ES, protein was extracted from HDFs using pro-prep TM (Cosmo Bio, Tokyo, Japan) according to the manufacturer's instruction. Pooled samples containing the same amount of protein were subjected to SDS-polyacrylamide gel electrophoresis (BIO-RAD, CA, USA) and transferred onto membranes (Thermo Fisher Scientific, MA, USA). After blocking with blocking reagents (GE Healthcare, Buckinghamshire, UK), the membranes were incubated overnight at 4°C with the following primary antibodies: anti-α-SMA antibody (ab5694; Abcam, Cambridge, UK) or anti-GAPDH antibody (G8795; Sigma-Aldrich, MO, USA). The membranes were then incubated with the appropriate secondary antibodies, anti-rabbit IgG antibody (NA934V; GE Healthcare) or anti-mouse IgG antibody (NA931V; GE Healthcare), for 1 h at room temperature. The membranes were incubated with ECL mix (GE Healthcare), and the blots were quantified by densitometry (Chemi Doc XRS; BIO-RAD). Western blotting was performed four times using pooled samples ($n = 4$ per group). Data were normalized using GAPDH and by relative expression and compared with levels in the control group with Image J (National Institutes of Health, Bethesda, MD, USA).

Collagen gel contraction assay

The collagen gel contraction assay was performed to analyze the contractile ability of HDFs using a collagen-based cell contraction assay kit (Cell Biolabs, CA, USA) according to the manufacturer's protocol. First, 240×10^4 cells were mixed with collagen solution and incubated for 1 h at 37°C. The solution was then added to 1 mL of DMEM and incubated for 48 h at 37°C in a CO_2 incubator. Collagen gels were separated from the dishes with spatula and subjected to ES for 24 h. Gel contractions were observed at 24 and 48 h after ES initiation. The gel areas were measured using image J and the area change rates were calculated for each dish.

Measurement of culture medium pH

pH was measured in each culture medium after ES. A pH probe (Mettler Toledo, Zurich, Switzerland) coupled with a pH meter (Mettler Toledo) was used to measure pH. The pH probe was calibrated with a standard pH buffer solution (pH 4.01, 6.86, and 9.18; AS ONE, Osaka, Japan) before immersing the probe in culture medium to measure pH.

Statistical analysis

All data were tested using the Shapiro-Wilk test and F-test. Student's t-tests were used to analyze the data that followed a normal distribution with equal variances, and the results with $p < 0.05$ were considered statistically significant. Bonferroni correction was used and $p < 0.0125$ was considered statistically significant when the data were compared among more than three groups. When the data did not follow a normal distribution, the Mann-Whitney U test was used to evaluate data. Results with $p < 0.05$ were considered statistically significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).

Ethical approval

In this study, we used a primary cell culture sold by Clonetics, and therefore, the study did not require ethical approval.

Results

ES with high duty cycle has adverse effects on HDFs

To better understand the adverse effect of ES on fibroblasts, we examined the cell viability and cell numbers after ES. Cell viability was decreased in the 50% and 90% groups ($p < 0.0125$ vs. control) and the viability of the 90% group was less than 90% (Fig. 3). However, ES with a 10% duty cycle did not decrease cell viability. Cell number after ES in the 90% group was decreased to less than 70%, but there were no significant differences between control and stimulus groups (v.s. 10%; $p = 0.237$, v.s. 50%; $p = 0.339$, and v.s. 90%; $p = 0.021$, respectively). These results indicate that cell toxicity might occur as the duty cycle approaches 100%, and direct current and high duty cycle could suppress cell proliferation. Next, to confirm ionization by ES, we measured the pH of each culture medium. The pH values of culture media were 7.77 ± 0.14 (control), 7.93 ± 0.09 (duty cycle 10%), 7.91 ± 0.05 (duty cycle 50%), and 7.96 ± 0.08 (duty cycle 90%), with no significant differences between the control and stimulus groups.

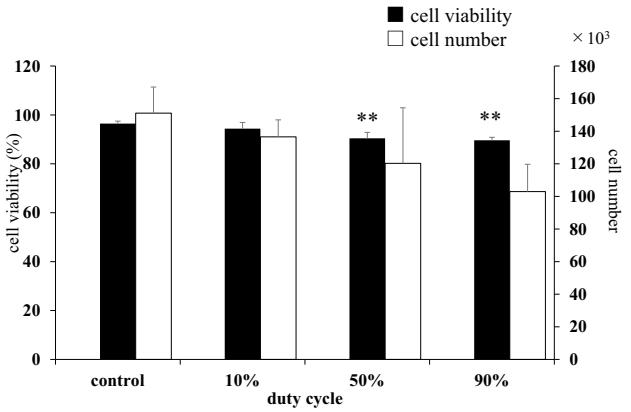

Fig. 3 Adverse effects of electrical stimulation on human dermal fibroblasts.
The cell viability of human dermal fibroblasts after electrical stimulation is shown. Data are presented as the mean ± SD; n = 4 per group. **, $p < 0.01$, significant difference between the electrical stimulation group and the control group. The statistical differences between the control and the treated groups were tested by Student's t-tests with a Bonferroni correction.

ES promotes the expression of α-SMA and TGF-β1

The mRNA and protein expression levels were compared between the control and the 10% groups because ES with a duty cycle of 50% and 90% introduced cell death. ES with a 10% duty cycle significantly promoted the mRNA expression of α-*SMA* and *TGF-β1* (Fig. 4, $p = 0.029$ and $p = 0.029$). The mRNA expression of α-*SMA* in the 10% group was more than twice that in the control group. The protein level of α-SMA in the 10% group was similarly significantly higher than that of the control group (Fig. 5, $p = 0.046$). Thus, ES with a duty cycle of 10% might promote the differentiation of fibroblasts into myofibroblasts.

ES promotes collagen gel contraction

To confirm the effect on wound closure, we investigated the contractile capacity of fibroblasts using the three-dimensional (3D) collagen gel contraction assay. Collagen gel contraction rates were compared between control and 10% groups. The areas of collagen gels were reduced after

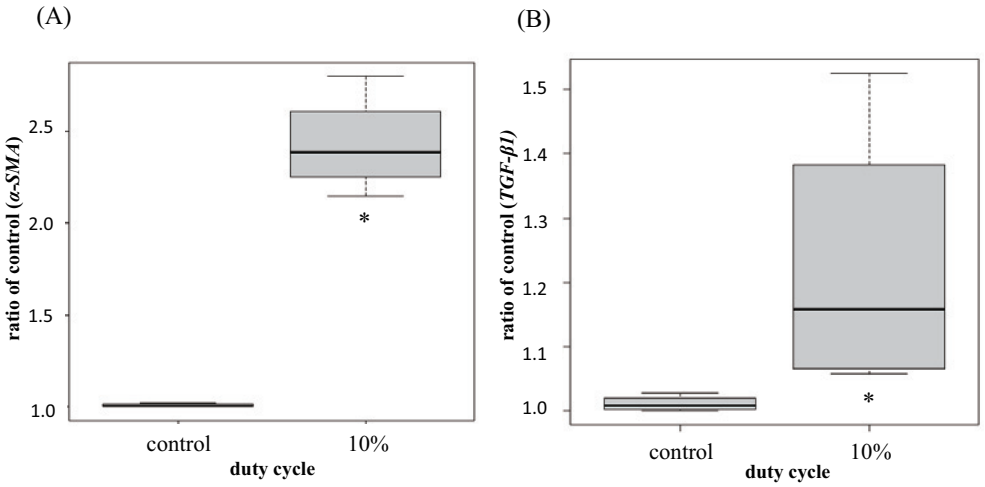

Fig. 4 The expression of *α-SMA* and *TGF-β1* in human dermal fibroblasts after electrical stimulation.
Relative expression of (A) *α-SMA* and (B) *TGF-β1* mRNA. Data are presented as box-whisker plots. The statistical differences between the control and the 10% group were tested by Mann-Whitney U test; n = 4 per group. *, $p < 0.05$, significant difference between the 10% group and the control group.

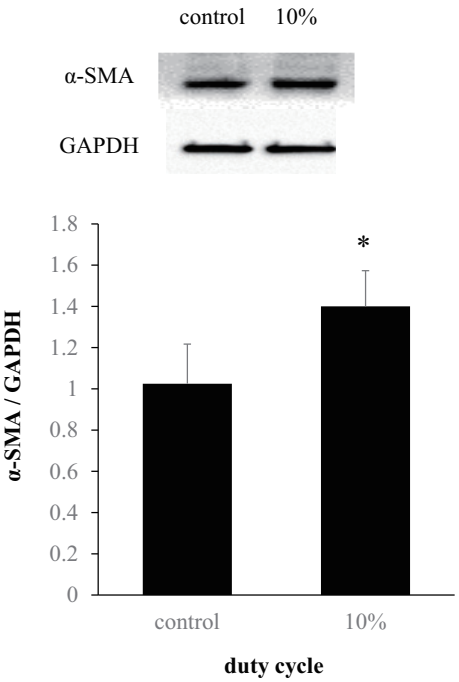

Fig. 5 α-SMA protein expression in human dermal fibroblasts after electrical stimulation.
(A) A representative blot is shown. (B) Western blot quantitation. Data are presented as box-whisker plots; n = 4 per group. The statistical difference between the control and the 10% group was tested by the Student's-t test.

stimulation (Fig. 6A). Fig. 6B, 6C show the rate of change in the gel areas since the beginning of ES in gels with HDFs contracted for 24 and 48 h. The gel subjected to ES with a 10% duty cycle contracted more than the control at 24 and 48 h after ES initiation ($p = 0.0096$, $p = 0.0115$, respectively), and the gel of the 10% group was contracted by approximately 50% from the beginning. These results indicate that ES of a 10% duty cycle promoted the contractile ability of HDFs with myofibroblast differentiation, and this was maintained both during and after ES.

Discussion

The present study showed a novel way to establish the optimum duty cycle of ES therapy for healing pressure injuries by analyzing the effects of duty cycle on HDFs. The monophasic-pulsed microcurrent of a 10% duty cycle promoted α-SMA and TGF-β1 expression and collagen gel contraction without cytotoxicity. These results suggest that a monophasic-pulsed current promotes fibroblast differentiation into myofibroblasts and that this effect is related to the duty cycle.

Viability of HDFs exposed to ES with a duty cycle of 50% and 90% was decreased to less than 90%, and cell number in the 90% group was decreased. This result indicated that an ES with a >50% duty cycle has toxic effects for HDFs. We hypothesized that the cell toxicity of ES was related to electrolysis and thus measured the pH of each culture medium. The pH of culture media in ES groups were alkalized (around 7.9), but there were no significant differences between control and ES groups. These results indicated that the cell toxicity of ES was not due to the change in pH. Some studies have shown that ES induces cell apoptosis and necrosis depending on voltage or pulse length with electroporation in the cell membrane and influx of Ca^{2+} [19-21]. Pulse length is decided by the duty cycle and a high duty cycle means a long pulse length. Thus, ES with a high duty cycle might alter the permeability of cell membranes, inducing cell death. Moreover, the pH of the wound surface is higher with severe pressure injury and the pH of the wound surface is increased when pressure injury deteriorates[22,23]. Therefore, it is necessary to use electrodes in which ionization tendency is large in clinical trials because ES might increase the pH of tissues to avoid alkalization of wound surface.

Regarding the contractile ability of HDFs with ES, that with a duty cycle of 10% promoted the contraction of collagen gel. Wang et al[14], who adopted 24-h ES, reported that duty cycle of approximately 8% (pulse width of 10 ms within 1200 ms) with 50 mV/mm promotes collagen gel contraction; however, duty cycle of 50% (pulse width of 300 ms within 600 ms) with 50 mV/mm did not promote this. This is similar to the result of the present study. However, ES with 100 mV/mm promoted collagen gel contraction in both conditions[14]. This could be due to the difference in intensity. Thus, duty cycle might be involved in the contractile ability of HDFs. ES with a duty cycle of 10% also promoted α-*SMA* and *TGF-β1* expression. As shown previously, α-SMA expression is an indicator of myofibroblast, and collagen gel contractile ability reflects wound contraction, which is necessary for wound closure. ES with a duty cycle of 10% promoted both α-SMA expression and collagen gel contraction. Thus, fibroblasts might differentiate into myofibroblasts with ES. Moreover, TGF-β1 is a key factor in wound contraction that functions by promoting α-SMA expression, differentiation, and the secretion of collagen[12]. The present study results suggest that ES might induce differentiation of myofibroblasts and wound contraction by autocrine secretion of TGF-β1 and α-SMA in HDFs. However, this study did not assess temporal changes in the expressions of mRNA and protein. α-SMA expression could be higher within 24 h after ES initiation, but the relationship between the expression of α-SMA and the duration of ES is unclear in this study. Yoshikawa et al[10] showed that 1-h ES with a duty cycle of 50% promotes cell proliferation. Thus, the pro-fibrotic effects of ES on HDFs might be influenced by stimulation duration. Moreover, it is not clear which cell sensor received ES to promote TGF-β1 and α-SMA expression. TGF-β1-mediated signals are enhanced via integrin β1, which is a cell surface receptor[24]

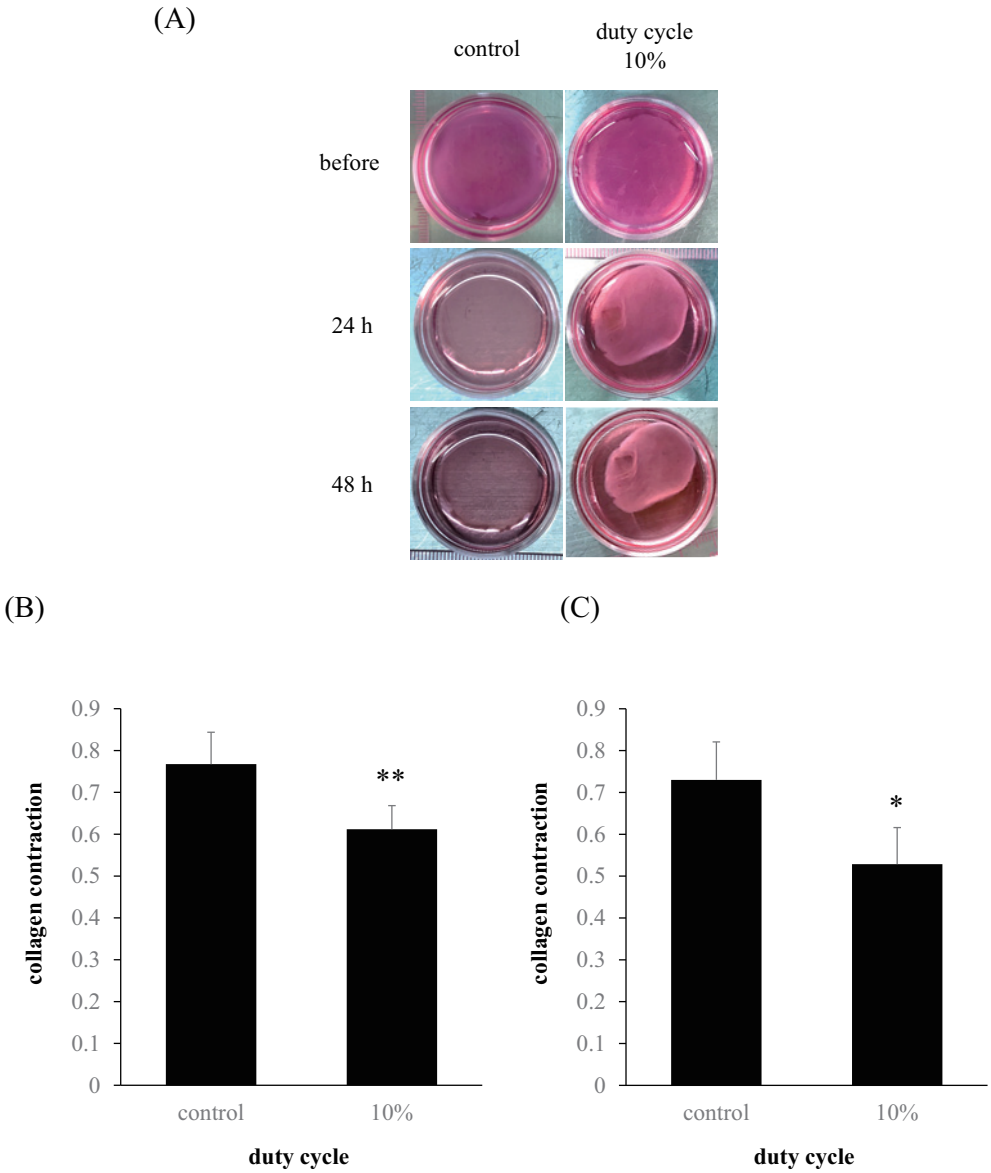

Fig. 6 Collagen gel contraction.

(A) The collagen gel contraction in human dermal fibroblasts 24 and 48 h after electrical stimulation (ES) initiation. (B) Quantification of collagen gel contraction 24 h after ES initiation. (C) Quantification of collagen gel contraction 48 h after ES initiation. Data are presented as the mean ± SD; n = 4 per group. **, $p < 0.01$, significant difference between the ES with a duty cycle of 10% group and the control group. The statistical difference between the control and the 10% group was tested by Student's t-test.

and contributes to some outside-in signals that regulate certain cellular functions including differentiation[25].

This study revealed that myofibroblast differentiation mediated by ES is influenced by duty cycle and that ES with a duty cycle of 10% promotes cell differentiation, whereas a duty cycle >50% induces cell death. Some studies revealed that difference in intensity or frequency affects cell behavior such as migration, proliferation, and the secretion of some cytokines[9,13,14,26]. Thus, the effects of ES on cell behavior differed with these parameters. In this study, we examined the effects of differences in the duty cycle on HDF differentiation into myofibroblasts and viability. The results indicated that a duty cycle of 10% promotes wound contraction with myofibroblast differentiation. However, a higher duty cycle and long-term stimulation might have adverse effects. Therefore, it is necessary to set stimulation parameters, such as duty cycle, duration, intensity, frequency, and polarity, according to the purpose of ES for pressure injuries in clinical trials.

Limitation

The reason for the decrease in cell viability in the 50% and 90% groups was unclear. A 24-h ES with a duty cycle

of 10% promoted myofibroblast differentiation, but this study used only 24-h stimulation and did not reveal the relationship between ES duration and fibrotic effects. Therefore, 10% might not be the optimum duty cycle for HDFs with short duration. *TGF-β1* mRNA expression was increased by ES with a duty cycle of 10%, but other cytokines and the signaling pathway that accelerates the secretion of fibrotic factors induced by ES are also unclear. Therefore, further study is needed to investigate the effect of duration on differentiation and which pathway is influenced by ES.

Conclusion

This study suggests that the duty cycle influences myofibroblast differentiation and HDF viability and shows that 10% is the effective duty cycle of monophasic-pulsed micro-currents for granulation tissue formation, which induces pressure injury healing.

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Conflict of Interest: The authors declare no conflicts of interest.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Association between Social Frailty and Sleep Quality among Community-dwelling Older Adults: A Cross-sectional Study

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ABSTRACT. Objective: We examined the association between social frailty and subjective sleep quality among community-dwelling adults. Methods: This cross-sectional study recruited Japanese adults over the age of 60 years from health check-ups held in a public townhall in a suburban area between 2018 and 2019. Social frailty was evaluated using five criteria (living alone, not visiting friends sometimes, going out less frequently than the last year, not feeling helpful to friends or family, and not talking to someone every day) and categorized into three groups: non-frailty, pre-frailty, and frailty. Sleep quality was assessed according to the Pittsburgh Sleep Quality Index (PSQI) by giving participants a self-reported questionnaire. We performed multivariable linear regression analysis, denoting social frailty as an independent variable, and the global PSQI score as a dependent variable. Results: Data from 300 older adults were analyzed, 51.0% of whom were female. The participants' mean age was 73.0 years (standard deviation = 5.8). Multivariable analysis revealed the notable association between social frailty and a high global PSQI score (compared with non-frailty, frailty: β = 0.94, 95% CI = 0.08 to 1.80, p = 0.033). Of the five determiners of social frailty, not talking with someone every day was especially associated with a high global PSQI score (β = 1.57, 95% CI = 0.49 to 2.66, p = 0.005). Conclusion: The present study suggests that social frailty is associated with poor sleep quality among community-dwelling older adults. Our findings indicate the importance of social frailty on sleep quality among older adults.

Key words: Older adults, Pittsburgh Sleep Quality Index, Sleep quality, Social frailty

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Poor sleep quality is one of the most common health issues in older adults. Approximately 50% of people older than 55 years suffer from sleep problems more frequently and severely than younger people[1,2]. Poor sleep quality among the older population is attributed to fatigue, reduction of quality of life, risk of cardiovascular disease, and mental health disorders[3-5]. In particular, it also seems to be associated with geriatric syndromes, such as cognitive impairment[6,7] and sarcopenia[8,9], which could be addressed by preventive physical therapy. Thus, sleep problems in adults have become a new area to explore through the lens of preventive physical therapy.

Sleep hygiene has been garnering attention as a non-pharmacological form of therapy to improve sleep quality. In Japan, a research team led by the Ministry of Health, Labour and Welfare published "Sleep Guidelines for Health Promotion 2014," which has been incorporated into sleep hygiene education across the country[10]. The guidelines mainly accredit healthy sleep to lifestyle factors like daytime physical activities[11], eating habits[12], and regular life rhythms[13], and also highlight the negative effects of alcohol[14], smoking[15], and caffeine consumption[16]. However, they do not elaborate upon the social factors impacting

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sleep quality.

Recently, some reports regarding older adults have indicated a connection between their social relationships and sleep quality. Rich social relationships improve mental health through stress-buffering, regularizing life rhythms, and promoting physical activities by meeting friends and going out, which in turn enhances sleep quality[17]. Several cross-sectional studies have shown that high social support is associated with good sleep quality[17,18] while social isolation and loneliness hamper the quality of sleep[19]. Moreover, in a longitudinal study, social isolation predicted poor sleep quality[20], suggesting the possibility that the quality of sleep among older adults is hindered by social vulnerability. On the other hand, another longitudinal study depicted no association between social participation and sleep quality[21]. Therefore, the results are inconsistent.

These previous studies have focused on the effects of only one or two aspects of social factors and may not capture the overall effects of social vulnerability. Consequently, Bunt et al. proposed social frailty as a multifaceted concept with respect to social vulnerability and the incorporation of social resources, social behaviors, and social activities[22]. Social frailty can provide a comprehensive view of older adults' social conditions, as opposed to assessing social factors from a single aspect, such as social isolation or lack of social support. However, few studies have examined the impact of social frailty on sleep quality. One cross-sectional study examined the association between sleep conditions and social frailty in community-dwelling Japanese older adults[23], but it only analyzed sleep duration and daytime wakefulness as sleep conditions; thus, it may not provide a holistic assessment of sleep quality.

Hence, the present study aimed to examine the association between social frailty and self-reported sleep quality among community-dwelling older adults. We hypothesized that social frailty was connected to poor sleep quality and assessed the importance of social frailty in addressing poor sleep quality among older adults.

Methods

Study population

The present cross-sectional study recruited Japanese older adults from the Togo town study carried out in cooperation with Nagoya University (Department of Integrated Health Sciences) and the Togo Town office. The community-based health check-up survey was conducted in the public town-hall of Togo town, a sub-urban area in Japan, in July and August of 2018 and 2019. Inclusion criteria required that the participants had lived in Togo Town, participated in the health check-up survey, and were independent in daily living. Exclusion criteria required that the participants under the age of 60 years and those who had dementia or depression disorder. Of the total 320 participants, we excluded people who lacked gender information (n = 1), were under 60 years of age (n = 13), and suffered from self-reported dementia (n = 3) or depression disorder (n = 3). Finally, we analyzed 300 older adults, all of whom provided written informed consent beforehand. The study protocol was approved by the ethics committee of Nagoya University (No. 18-502) and conducted according to the guidelines of the Declaration of Helsinki.

Outcome measure: sleep quality

Sleep quality was assessed using a self-administered questionnaire, the Pittsburgh Sleep Quality Index (PSQI)[24,25], in tandem with a Japanese version[26,27]. The PSQI focuses on sleep quality during the previous month, and consists of seven subcomponents: subjective sleep quality, sleep latency (the time it takes to fall asleep), sleep duration, habitual sleep efficiency (the ratio of total sleep time to time in bed), sleep disturbances, the use of sleep-promoting medication (prescribed or over-the-counter), and daytime dysfunction. Each sub-component is scored from 0 to 3 points, with a total of 21 points (global PSQI score). Notably, higher scores indicate poorer sleep quality. A previous study has shown a global PSQI score cut-off (5.5 points) for reduced sleep quality[26]. However, because there were somewhat small numbers of eligible study participants (n = 57), the present study used the global PSQI score as a continuous variable. We also assessed the symptoms during sleep that could be associated with sleep disorders using the additional items of the PSQI questionnaire: loud snoring ("snoring loudly") and sleep apnea ("long pauses between breaths while asleep"), restless leg syndrome ("legs twitching or jerking while asleep"), and parasomnia ("episodes of disorientation or confusion during sleep"). We identified participants who depicted these symptoms objectively, while sleeping in the same bedroom as their roommates: loud snoring (n = 9), sleep apnea (n = 5), and restless leg syndrome (n = 5). None of them reported experiencing parasomnia.

Exposure measure: social frailty

Based on a previous study[28], social frailty was assessed using five items on a self-reported questionnaire: living alone, not visiting their friends sometimes, going out less frequently than the last year, not feeling helpful to friends or family, and not talking to someone every day. Participants were allocated into three groups based on how many items applied to them: non-frailty (none), pre-frailty (one), and frailty (two or more).

Covariates

A self-reported questionnaire recorded sociodemographic characteristics: age, gender, body mass index (BMI), educational attainment, household equivalent income, working status, present illnesses, instrumental activities of

daily living (IADL), smoking, drinking, frequent urination, physical activity, and depressive symptoms. Age, BMI, household equivalent income, and physical activities were treated as continuous variables. BMI was calculated from height and weight measured using a multifrequency bioelectrical impedance analyzer (MC-780A, Tanita, Tokyo, Japan). Meanwhile, educational attainment was categorized as follows: <9, 10 to 12, and ≥13 years. Household equivalent income was evaluated by dividing the income of each household by the square root of the household size (number of family members). Working status was dichotomized as "not working" and "working." Present illnesses were assessed using a question that asked respondents whether they had received a diagnosis of cancer, heart disease, stroke, respiratory disease, hypertension, dyslipidemia, or diabetes. Respondents indicated "yes" or "no" in response to each illness. IADL was measured using a five-item subscale of the Tokyo Metropolitan Institute of Gerontology Higher Competence Scale[29]. We categorized participants who had difficulty with at least one item as "with difficulty," and others as "without difficulty." Drinking and smoking were also dichotomized as "no" and "yes," respectively. Frequent urination was assessed by the frequency of urination daytime (8 times or more/day) and nighttime (once or more/day), dichotomized as "no" (none) and "yes" (either daytime or nighttime). Physical activity was gauged using a simplified version of the International Physical Activity Questionnaire[30]. Depressive symptoms was assessed using the 15 items of the Depression Geriatrics Scale, and those who scored five or more were denoted as "with depressive symptoms."[31] Since physical activity and depression were considered intermediate factors, they were not included in the main analytical model.

Statistical analysis

First, descriptive statistics were calculated to summarize the participants' characteristics according to the social frailty category. Second, we calculated the descriptive statistics regarding the PSQI score for each of the five components of social frailty. Third, to examine the association between social frailty and sleep quality, we applied multivariable linear regression analysis and obtained unstandardized regression coefficients (βs) and 95% confidence intervals (CIs) on the global PSQI score. We used social frailty as an explanatory variable. For the main analytical model, we performed the analysis using a crude model and a multivariable-adjusted model with covariates of potential confounders (age, gender, education, income, employment status, present illness, IADL, BMI, drinking, smoking, and frequent urination). Next, we also made evaluations including physical activity and depression in the analytical model. In addition, we conducted an analysis using social frailty subcomponents as explanatory variables in the same statistical model; the five subcomponents were simultaneously introduced into the analytical model. For the sensitivity analysis, we excluded those who potentially showed objective symptoms related to sleep disorders (loud snoring, sleep apnea, and restless leg syndrome) and confirmed the results.

To mitigate any potential bias caused by missing information, we used the multiple imputation approach under the missing at random (MAR) assumption (i.e., the missing data mechanism depends only on the observed variables). We generated 20 imputed datasets by utilizing the Multiple Imputation by Chained Equations (MICE) procedure and pooled the results using the standard Rubin's rule[32].

We used R software (Version 3.6.3 for Windows) for all statistical analyses, setting the significance level at $p < 0.05$. The multiple imputation approach used the MICE function (mice package).

Results

In total, we evaluated 300 participants, whose characteristics are shown in Table 1. The mean age of participants was 73.0 (standard deviation = 5.8) years, and 153 (51.0%) were women. Regarding social frailty, 152 (50.7%) participants displayed characteristics of non-frailty, 82 (27.3%) of pre-frailty, and 52 (17.3%) of frailty. Socially frail individuals were likely to be older, male, less educated, and have lower household equivalent income, with a diagnosis of diabetes, but not stroke or respiratory disease. They also showed signs of being prone to IADL difficulty. In addition, individuals with greater social frailty had a longer sleep duration and higher global PSQI score.

Table 2 shows the descriptive statistics for the PSQI scores for each of the five sub-items of social frailty. Sleep duration was reported to be longer for participants who recorded not visiting friends sometimes, or not feeling helpful toward friends or family. As for the global PSQI score, the scores were higher for individuals who did not feel helpful toward friends or family, or did not talk to someone every day.

Table 3 shows the findings for the association between social frailty and global PSQI score. Multivariable linear regression analysis revealed that social frailty was significantly associated with a higher PSQI score when compared with non-frailty - after adjustment for all covariates of potential confounders (pre-frailty: β = 0.02, 95% CI = -0.69 to 0.73, $p = 0.958$; frailty: β = 0.93, 95% CI = 0.08 to 1.79, $p = 0.033$). In addition, the PSQI score was significantly higher as the number of social frailty items increased (p for trend = 0.030). Table 4 shows the association between social frailty subcomponents and global PSQI score. Among the five items of social frailty, not talking to someone every day showed a notable association with regard to a higher PSQI score (β = 1.64, 95% CI = 0.55 to 2.72, $p = 0.003$). Even when the sensitivity analysis was performed, exclud-

Table 1. Participants' characteristics

		Social frailty*			
		Non-frailty	Pre-frailty	Frailty	*P*-value†
		n = 152	n = 82	n = 52	
Age (years), mean (SD)		72.2 (5.5)	73.0 (5.6)	75.1 (6.7)	0.008
Gender, n (%)	Male	71 (46.7)	38 (46.3)	27 (51.9)	0.783
	Female	81 (53.3)	44 (53.7)	25 (48.1)	
BMI (kg/m^2), mean (SD) *		22.3 (2.7)	22.7 (2.9)	22.8 (3.6)	
Educational attainment (years), n (%)	Under 9	17 (11.2)	16 (19.5)	10 (19.2)	0.098
	10 to 12	66 (43.4)	34 (41.5)	28 (53.8)	
	13 or more	69 (45.4)	31 (37.8)	14 (26.9)	
	Missing	0 (0.0)	1 (1.2)	0 (0.0)	
Household equivalent income (10,000 JPY), mean (SD) *		293.3 (122.0)	240.6 (130.5)	213.3 (83.3)	< 0.001
Working status, n (%)	Not working	138 (90.8)	72 (87.8)	49 (94.2)	0.353
	Working	14 (9.2)	9 (11.0)	2 (3.8)	
	Missing	0 (0.0)	1 (1.2)	1 (1.9)	
Present illness, n (%)					
Cancer	No	142 (93.4)	75 (91.5)	49 (94.2)	0.830
	Yes	5 (3.3)	4 (4.9)	2 (3.8)	
	Missing	5 (3.3)	3 (3.7)	1 (1.9)	
Heart disease	No	137 (90.1)	75 (91.5)	47 (90.4)	0.802
	Yes	10 (6.6)	4 (4.9)	4 (7.7)	
	Missing	5 (3.3)	3 (3.7)	1 (1.9)	
Stroke	No	140 (92.1)	76 (92.7)	50 (96.2)	0.674
	Yes	7 (4.6)	3 (3.7)	1 (1.9)	
	Missing	5 (3.3)	3 (3.7)	1 (1.9)	
Respiratory disease	No	137 (90.1)	76 (92.7)	49 (94.2)	0.555
	Yes	10 (6.6)	3 (3.7)	2 (3.8)	
	Missing	5 (3.3)	3 (3.7)	1 (1.9)	
Hypertension	No	94 (61.8)	55 (67.1)	28 (53.8)	0.263
	Yes	58 (38.2)	26 (31.7)	24 (46.2)	
	Missing	0 (0.0)	1 (1.2)	0 (0.0)	
Dyslipidemia	No	99 (65.1)	53 (64.6)	31 (59.6)	0.746
	Yes	53 (34.9)	28 (34.1)	21 (40.4)	
	Missing	0 (0.0)	1 (1.2)	0 (0.0)	
Diabetes	No	141 (92.8)	69 (84.1)	43 (82.7)	0.067
	Yes	11 (7.2)	12 (14.6)	9 (17.3)	
	Missing	0 (0.0)	1 (1.2)	0 (0.0)	
IADL, n (%)	Without difficulty	149 (98.0)	78 (95.1)	45 (86.5)	0.004
	With difficulty	3 (2.0)	4 (4.9)	7 (13.5)	
Drinking, n (%)	No	88 (57.9)	46 (56.1)	34 (65.4)	0.572
	Yes	64 (42.1)	35 (42.7)	18 (34.6)	
	Missing	0 (0.0)	1 (1.2)	0 (0.0)	
Smoking, n (%)	No	143 (94.1)	76 (92.7)	48 (92.3)	0.901
	Yes	9 (5.9)	5 (6.1)	4 (7.7)	
	Missing	0 (0.0)	1 (1.2)	0 (0.0)	
Frequent urination, n (%)	No	20 (13.2)	10 (12.2)	3 (5.8)	0.368
	Yes	131 (86.2)	71 (86.6)	49 (94.2)	
	Missing	1 (0.7)	1 (1.2)	0 (0.0)	
Physical activities (Mets hour/day), mean (SD) *		5.4 (7.4)	5.7 (8.0)	4.3 (5.4)	0.553

Table 1. Participants' characteristics (continued)

		Social frailty*			*P*-value†
		Non-frailty	Pre-frailty	Frailty	
		n = 152	n = 82	n = 52	
Depressive symptoms, n (%)	No	133 (87.5)	62 (75.6)	27 (51.9)	< 0.001
	Yes	8 (5.3)	11 (13.4)	19 (36.5)	
	Missing	11 (7.2)	9 (11.0)	6 (11.5)	
Sleep duration (hours/day), mean (SD) *		7.2 (1.0)	7.5 (1.3)	7.6 (1.4)	0.016
Global PSQI score, mean (SD) *		4.0 (2.4)	3.9 (2.6)	4.8 (2.9)	0.134
PSQI subitem score, mean (SD) *					
Subjective sleep quality		1.2 (0.7)	1.2 (0.6)	1.3 (0.7)	0.593
Long sleep latency		0.8 (0.9)	0.8 (1.0)	1.2 (1.2)	0.038
Short sleep duration		0.4 (0.7)	0.3 (0.7)	0.3 (0.7)	0.598
Low habitual sleep efficiency		0.03 (0.2)	0.01 (0.11)	0.1 (0.4)	0.090
Sleep disturbances		0.8 (0.5)	0.8 (0.6)	1.1 (0.6)	0.004
Use of sleep-promoting medication		0.3 (0.8)	0.3 (0.8)	0.4 (1.0)	0.543
Daytime dysfunction		0.4 (0.6)	0.6 (0.7)	0.5 (0.6)	0.130

BMI: body mass index; IADL: instrumental activities of daily living; PSQI: Pittsburgh Sleep Quality Index; SD: standard deviation
*Missing data: social frailty, n = 14; BMI, n = 1; household equivalent income, n = 26; physical activities, n = 27; sleep duration, n = 6; global PSQI score, n = 57; subjective sleep quality, n = 7; long sleep latency, n = 22; short sleep duration, n = 6; low habitual sleep efficiency, n = 19; sleep disturbances, n = 21; use of sleep-promoting medication, n = 8; daytime dysfunction, n = 10
†Continuous variables were analyzed by analysis of variance, and categorical variables were analyzed by chi-square tests

ing those suspected of having sleep-related disorders (loud snoring, sleep apnea, or restless leg syndrome), the association between social frailty and PSQI score exemplified little variation (Supplementary Table 1 and 2). On the other hand, the significant connection between social frailty and sleep quality diminished upon introduction of the analytical model of depressive symptoms (Supplementary Table 3 and 4).

Discussion

In the present cross-sectional study, we investigated the consequence of social frailty on sleep quality among older adults living in a community. Social frailty was associated with poor sleep quality; not talking with someone every day had a particularly strong effect. Our findings suggest that rich social relationships could be beneficial for older adults' sleep quality.

Several previous studies have specified that flourishing social relationships through social support[17,18], and reduced social isolation[19,20] and loneliness[19] can improve sleep quality. Our results also corroborated this association in terms of social frailty, substantiating previous studies. According to Japan's Sleep Guidelines for Health Promotion 2014[10], the positive outcomes of daily exercise habits[11], eating habits[12], and regular life rhythm[13], as well as the ramifications of alcohol[14], smoking[15], and caffeine[16] on sleep quality are considered as contributive lifestyle habits. Besides, our analyses prompt the notion of addressing social frailty to foster sleep hygiene in older adults.

Social frailty can find many pathways to potentially impair sleep quality, one of which may be through deteriorating mental health, stemming from insufficient social support, low physical activity, and irregular life rhythms due to a lack of daytime social activities. In our supplementary analysis, adding the intermediate variables to the analytical model showed that depressive symptoms could justify many of the associations between social frailty and poor sleep quality. Therefore, addressing social frailty might contribute to better sleep quality by improving mental health. However, the association between social vulnerability, such as social isolation and depressive symptoms, is known to be bidirectional[33]. Because the present study employed a cross-sectional design, it was difficult to separate confounding and mediating effects of depressive symptoms, so the results should be interpreted with caution. Therefore, further investigations using longitudinal panel data are necessary.

Of the sub-items, not talking with someone every day had a significant effect on poor sleep quality. Social relationships have two aspects: structural factors like social networks or participation in organizations - all of which are quantity-based - the quality-based functional elements, such as social support and social interactions[34]. Among social frailty subcomponents, living alone, frequency of going out, and visiting friends are categorized as structural aspects of social relationships, while talking with someone and holding perceptions of helping friends and family are cate-

Table 2. PSQI score for each component of social frailty

	Social frailty subcomponents*														
	Living alone			Sometimes visiting friends			Going out less frequently than the last year			Feeling helpful toward friends or family			Talking with someone every day		
	No	Yes		Yes	No		No	Yes		Yes	No		Yes	No	
	n = 243	n = 48	*P*-value†	n = 225	n = 73	*P*-value†	n = 258	n = 40	*P*-value†	n = 265	n = 31	*P*-value†	n = 260	n = 34	*P*-value†
Sleep duration (hours/day), mean (SD) *	7.4 (1.1)	7.4 (1.6)	0.985	7.2 (1.1)	7.7 (1.3)	0.004	7.3 (1.2)	7.5 (1.3)	0.311	7.3 (1.2)	7.7 (1.4)	0.084	7.4 (1.2)	7.4 (1.3)	0.965
Global PSQI score, mean (SD) *	4.0 (2.4)	4.7 (3.0)	0.147	4.0 (2.6)	4.2 (2.4)	0.563	4.1 (2.5)	3.8 (2.6)	0.602	3.9 (2.4)	4.9 (3.2)	0.085	3.8 (2.4)	5.6 (3.0)	0.001
PSQI subitem score, mean (SD) *															
Subjective sleep quality	1.2 (0.7)	1.4 (0.7)	0.090	1.2 (0.7)	1.2 (0.6)	0.906	1.2 (0.7)	1.1 (0.6)	0.365	1.2 (0.7)	1.2 (0.7)	0.720	1.2 (0.6)	1.4 (0.7)	0.070
Long sleep latency	0.8 (0.9)	1.2 (1.2)	0.025	0.9 (1.0)	0.9 (1.0)	0.505	0.9 (1.0)	0.8 (1.0)	0.469	0.9 (0.9)	1.1 (1.2)	0.127	0.8 (0.9)	1.4 (1.2)	< 0.001
Short sleep duration	0.4 (0.7)	0.5 (0.9)	0.151	0.4 (0.7)	0.3 (0.7)	0.100	0.4 (0.7)	0.4 (0.7)	0.866	0.4 (0.7)	0.3 (0.7)	0.409	0.4 (0.7)	0.4 (0.8)	0.676
Low habitual sleep efficiency	0.03 (0.2)	0.1 (0.4)	0.018	0.04 (0.2)	0.04 (0.2)	0.856	0.04 (0.2)	0.1 (0.3)	0.746	0.04 (0.2)	0.03 (0.2)	0.878	0.03 (0.2)	0.1 (0.4)	0.021
Sleep disturbances	0.8 (0.6)	1.0 (0.6)	0.084	0.8 (0.6)	0.9 (0.6)	0.232	0.8 (0.5)	1.0 (0.7)	0.028	0.8 (0.5)	1.0 (0.7)	0.055	0.8 (0.6)	1.2 (0.5)	< 0.001
Use of sleep-promoting medication	0.3 (0.8)	0.3 (0.9)	0.794	0.3 (0.8)	0.3 (0.8)	0.975	0.3 (0.8)	0.2 (0.7)	0.491	0.3 (0.8)	0.5 (1.0)	0.269	0.3 (0.8)	0.6 (1.1)	0.038
Daytime dysfunction	0.5 (0.7)	0.4 (0.5)	0.591	0.4 (0.6)	0.6 (0.7)	0.051	0.5 (0.7)	0.4 (0.5)	0.513	0.4 (0.6)	0.7 (0.8)	0.043	0.5 (0.7)	0.5 (0.6)	0.921

PSQI: Pittsburgh Sleep Quality Index; SD: standard deviation

*Missing data: living alone, n = 9; sometimes visiting friends, n = 2; going out less frequently compared with last year, n = 2; feeling helpful toward friends or family, n = 4; talking with someone every day, n = 6; global PSQI score, n = 57; average sleep duration, n = 6; subjective sleep quality, n = 7; long sleep latency, n = 22; short sleep duration, n = 6; low habitual sleep efficiency, n = 19; sleep disturbances, n = 21; use of sleep-promoting medication, n = 8; daytime dysfunction, n = 10

†Analyzed by Student's t-test

Table 3. Association between social frailty and global PSQI score using multivariable linear regression analysis with multiple imputation approach (n = 300)

	Crude model		Adjusted model[a]	
	β (95% CI)	*P*-value	β (95% CI)	*P*-value
Social frailty				
Non-frailty	Reference		Reference	
Pre-frailty	0.05 (-0.62, 0.72)	0.890	0.02 (-0.69, 0.73)	0.958
Frailty	0.92 (0.14, 1.71)	0.022	0.93 (0.08, 1.79)	0.033
	P for trend = 0.017[b]		*P* for trend = 0.030[b]	

β: unstandardized regression coefficients; CI: confidence interval; PSQI: Pittsburgh Sleep Quality Index

[a]Adjusted model included all covariates in the analytical model: age, gender, education, income, employment status, present illness, instrumental activities of daily living, body mass index, drinking, smoking, and frequent urination

[b]Per one of the components of social frailty

Table 4. Association between social frailty subcomponents and global PSQI score using multivariable linear regression analysis with multiple imputation approach (n = 300)

	Crude model		Adjusted model[a]	
	β (95% CI)	*P*-value	β (95% CI)	*P*-value
Social frailty subcomponent				
Living alone (ref: no)	0.02 (-0.83, 0.87)	0.964	-0.04 (-0.92, 0.84)	0.934
Sometimes visiting friends (ref: yes)	0.04 (-0.63, 0.71)	0.906	0.09 (-0.63, 0.80)	0.814
Going out less frequently compared with last year (ref: no)	-0.56 (-1.41, 0.28)	0.191	-0.53 (-1.41, 0.35)	0.241
Feeling helpful toward friends or family (ref: yes)	0.29 (-0.68, 1.26)	0.555	0.27 (-0.75, 1.29)	0.605
Talking with someone everyday (ref: yes)	1.65 (0.61, 2.68)	0.002	1.64 (0.55, 2.72)	0.003

β: unstandardized regression coefficients; CI: confidence interval; PSQI: Pittsburgh Sleep Quality Index

[a]Adjusted model included all covariates in the analytical model: age, gender, education, income, employment status, present illness, instrumental activities of daily living, body mass index, drinking, smoking, and frequent urination

gorized as functional aspects. The key to addressing older adults' sleep quality may lie in the functional aspects of social relationships rather than just the structural aspects. For instance, engaging in conversation as an exchange of social support may alleviate loneliness and offer a buffer from psychological stress. Sleep quality might be safeguarded particularly by receiving emotional support, such as asking others to listen to worries and complaints[35], rather than by providing social support, such as having a social role. Therefore, it might be important to develop relationships and communities that foster emotional support. However, since these are only speculations, further research is needed to identify the detailed mechanisms.

Our findings suggest the importance of social factors in older adults' sleep hygiene, given the large proportion of this population suffering from sleep-related issues, and the correlation of poor sleep quality to geriatric syndromes such as cognitive impairment[6,7] and sarcopenia[8,9]. Since these geriatric syndromes are major targets of preventive physical therapy, therapists also need to consider the significance of older adults' sleep quality. In addition to sleep hygiene approaches, such as improving daytime physical activity and regularizing life rhythms, improvement in social frailty through physical therapists' efforts can contribute to boosting older adults' sleep quality. For instance, therapists would be expected to help older adults build social relationships and promote the exchange of social support in community activities, such as "Kayoino-ba,"[36,37] which is the population measure for long-term care prevention by Japanese central and local governments. We believe that contributions of therapists to community approaches to address social frailty could also be essential for older adults' sleep hygiene.

Our study has several limitations that should be noted. First, the study's cross-sectional nature means there was potential for reversal of causality, so further studies using longitudinal data are needed. Second, sleep quality was assessed using a self-administered questionnaire, creating the possibility of measurement errors. Thus, further investigations with objective measurements for sleep quality are

needed, which can be done by utilizing devices such as actigraphs. Third, we did not have any information regarding the diagnosis of diseases related to sleep disorders. However, we did perform a sensitivity analysis, excluding participants portraying symptoms that alluded to sleep disorders, assessed from the additional PSQI items (loud snoring, sleep apnea, and restless leg syndrome); the results were almost the same. Therefore, we confirmed the robustness of our outcomes. Fourth, although adjusting the employment status based on the analytical model, we did not consider the participants' work hours (i.e., shifts). This may have confounded our results. Fifth, we had no information about participants' medication, so we could not consider it in the analysis. For instance, antidepressants and antianxiety medications can affect sleep quality. To address these issues, we excluded participants with self-reported depression disorder from the analysis. However, residual confounding is possible. Sixth, we used a social frailty index to examine the overall social vulnerability to sleep. However, there is still some disagreement over the definition of social frailty and the determination method[38]. Although the definition of social frailty requires further debate, we were able to examine sleep from a multifaceted social perspective. Finally, participants in our study were recruited out of convenience, chosen from among individuals participating in health check-ups held in a suburban town-hall. These participants were healthier and younger than typical community-dwelling older people living in the town, which might reduce the generalizability of our results. In fact, only a few people had a higher PSQI score than the cut-off, and even those with social frailty had an average score below the cut-off point. Therefore, our results were applicable to healthy older adults whose sleep quality was not severely impaired, so it should be noted whether our results apply to the general population of older adults.

Conclusion

The present study supported the notion that social frailty was associated with poor sleep quality. Our results imply that promoting rich social relationships could be vital to improving sleep quality. Since sleep quality is associated with geriatric syndromes, which can be the target of preventive physical therapy, it would be essential to develop rich social relationships in order to address older adults' sleep quality.

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Authors' contributions: TN conceptualized and designed the study, collected the data, analyzed the data, and drafted and revised the manuscript. IN contributed to data collection, and reviewed and critically revised the manuscript. TI-H contributed to data collection, and reviewed and critically revised the manuscript. HS, project administer, contributed to data collection, and reviewed and critically revised the manuscript. All authors read and approved the final manuscript.

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Supplementary material (Appendix):

1. Supplementary Table 1. Association between social frailty and global PSQI score excluding participants with symptoms related to sleep disorders, multivariable regression analysis with multiple imputation
2. Supplementary Table 2. Association between social frailty subcomponents and global PSQI score excluding participants with symptoms related to sleep disorders, multivariable regression analysis with multiple imputation
3. Supplementary Table 3. Association between social frailty and global PSQI score, including intermediate variables, multivariable linear regression analysis with multiple imputation (n = 300)
4. Supplementary Table 4. Association between social frailty subcomponents and global PSQI score, including intermediate variables, multivariable linear regression analysis with multiple imputation (n = 300)

Supplementary Table 1. Association between social frailty and global PSQI score excluding participants with symptoms related to sleep disorders, multivariable regression analysis with multiple imputation

	Excluding those with loud snoring (analyzed, n = 291)		Excluding those with sleep apnea (analyzed, n = 295)		Excluding those with restless leg syndrome (analyzed, n = 295)	
	Adjusted model		Adjusted model		Adjusted model	
	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value
Social frailty						
Non-frailty	Reference		Reference		Reference	
Pre-frailty	0.03 (-0.69, 0.75)	0.934	0.04 (-0.67, 0.75)	0.911	0.05 (-0.66, 0.76)	0.886
Frailty	0.95 (0.07, 1.82)	0.034	0.97 (0.11, 1.83)	0.028	0.98 (0.12, 1.85)	0.027
	P for trend = 0.030[a]		*P* for trend = 0.024[a]		*P* for trend = 0.023[a]	

ß, unstandardized regression coefficients; CI, confidence interval; PSQI, Pittsburgh Sleep Quality Index

[a]Per one of the components of social frailty

Analytical model was included all covariates in the analytical model: age, gender, education, income, working status, present illness, instrumental activities of daily living, body mass index, drinking, smoking, and frequent urination

Supplementary Table 2. Association between social frailty subcomponents and global PSQI score excluding participants with symptoms related to sleep disorders, multivariable regression analysis with multiple imputation

	Excluding those with loud snoring (analyzed, n = 291)		Excluding those with sleep apnea (analyzed, n = 295)		Excluding those with restless leg syndrome (analyzed, n = 295)	
	Adjusted model		Adjusted model		Adjusted model	
	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value
Social frailty subcomponents						
Living alone (ref: no)	-0.02 (-0.92, 0.88)	0.968	-0.02 (-0.91, 0.88)	0.972	-0.01 (-0.88, 0.87)	0.991
Sometimes visiting friends (ref: yes)	0.06 (-0.67, 0.78)	0.881	0.09 (-0.63, 0.81)	0.808	0.07 (-0.65, 0.79)	0.854
Going out less frequently compared with last year (ref: no)	-0.58 (-1.47, 0.32)	0.208	-0.52 (-1.41, 0.36)	0.247	-0.56 (-1.45, 0.33)	0.220
Feeling helpful toward friends or family (ref: yes)	0.27 (-0.75, 1.30)	0.600	0.26 (-0.75, 1.28)	0.613	0.27 (-0.74, 1.29)	0.600
Talking with someone everyday (ref: yes)	1.69 (0.59, 2.79)	0.003	1.69 (0.60, 2.78)	0.003	1.73 (0.64, 2.81)	0.002

ß, unstandardized regression coefficients; CI, confidence interval; PSQI, Pittsburgh Sleep Quality Index
Analytical model included all covariates: age, gender, education, income, working status, present illness, instrumental activities of daily living, body mass index, drinking, smoking, and frequent urination

Supplementary Table 3. Association between social frailty and global PSQI score, including intermediate variables, multivariable linear regression analysis with multiple imputation (n = 300)

	Model 1		Model 2		Model 3		Model 4	
	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value
Social frailty								
Non-frailty	Reference		Reference		Reference		Reference	
Pre-frailty	0.02 (-0.69, 0.73)	0.958	0.01 (-0.69, 0.72)	0.974	-0.05 (-0.76, 0.65)	0.881	-0.06 (-0.76, 0.65)	0.872
Frailty	0.93 (0.08, 1.79)	0.033	0.89 (0.03, 1.75)	0.044	0.63 (-0.27, 1.53)	0.172	0.60 (-0.31, 1.50)	0.198
	P for trend = 0.030[a]		*P* for trend = 0.039[a]		*P* for trend = 0.202 [a]		*P* for trend = 0.225 [a]	

ß, unstandardized regression coefficients; CI, confidence interval; PSQI, Pittsburgh Sleep Quality Index

[a]Per one of the components of social frailty

Model 1: adjusted by age, gender, education, income, working status, present illness, instrumental activities of daily living, body mass index, smoking, drinking, and frequent urination (reshown)

Model 2: adjusted by covariates in the Model 1 + physical activities

Model 3: adjusted by covariates in the Model 1 + depressive symptoms

Model 4: adjusted by covariates in the Model 1 + physical activities and depressive symptoms

Supplementary Table 4. Association between social frailty subcomponents and global PSQI score, including intermediate variables, multivariable linear regression analysis with multiple imputation (n = 300)

	Model 1		Model 2		Model 3		Model 4	
	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value	ß (95% CI)	*P*-value
Social frailty subcomponents								
Living alone (ref: no)	-0.04 (-0.92, 0.84)	0.934	-0.04 (-0.92, 0.84)	0.927	-0.01 (-0.89, 0.87)	0.978	-0.02 (-0.90, 0.87)	0.971
Sometimes visiting friends (ref: yes)	0.09 (-0.63, 0.80)	0.814	0.04 (-0.68, 0.75)	0.913	0.03 (-0.69, 0.75)	0.941	-0.01 (-0.73, 0.70)	0.971
Going out less frequently compared with last year (ref: no)	-0.53 (-1.41, 0.35)	0.241	-0.56 (-1.44, 0.32)	0.214	-0.71 (-1.61, 0.19)	0.124	-0.73 (-1.63, 0.17)	0.111
Feeling helpful toward friends or family (ref: yes)	0.27 (-0.75, 1.29)	0.605	0.22 (-0.80, 1.24)	0.679	-0.10 (-1.17, 0.97)	0.853	-0.14 (-1.21, 0.93)	0.801
Talking with someone everyday (ref: yes)	1.64 (0.55, 2.72)	0.003	1.68 (0.59, 2.76)	0.003	1.50 (0.41, 2.58)	0.007	1.54 (0.46, 2.63)	0.006

ß, unstandardized regression coefficients; CI, confidence interval; PSQI, Pittsburgh Sleep Quality Index
Model 1: adjusted by age, gender, education, income, working status, present illness, instrumental activities of daily living, body mass index, smoking, drinking, and frequent urination (reshown)
Model 2: adjusted by covariates in the Model 1 + physical activities
Model 3: adjusted by covariates in the Model 1 + depressive symptoms
Model 4: adjusted by covariates in the Model 1 + physical activities and depressive symptoms

PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Anatomical Increased/Decreased Changes in the Brain Area Following Individuals with Chronic Traumatic Complete Thoracic Spinal Cord Injury

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ABSTRACT. Objectives: This study aimed to investigate anatomical changes in the brain following chronic complete traumatic thoracic spinal cord injury (ThSCI) using voxel-based morphometry (VBM). That is, it attempted to examine dynamic physical change following thoracic injury and the presence or absence of regions with decreased and increased changes in whole brain volume associated with change in the manner of how activities of daily living are performed. Methods: Twelve individuals with chronic traumatic complete ThSCI (age; 21-63 years, American Spinal Injury Association Impairment Scale; grade C-D) participated in this study. VBM was used to investigate the regions with increased volume and decreased volume in the brain in comparison with healthy control individuals. Results: Decreases in volume were noted in areas associated with motor and somatosensory functions, including the right paracentral lobule (PCL)—the primary motor sensory area for lower limbs, left dorsal premotor cortex, and left superior parietal lobule (SPL). Furthermore, increased gray matter volume was noted in the primary sensorimotor area for fingers and arms, as well as in higher sensory areas. Conclusions: Following SCI both regions with increased volume and regions with decreased volume were present in the brain in accordance with changes in physical function. Using longitudinal observation, anatomical changes in the brain may be used to determine the rehabilitation effect by comparing present cases with cases with cervical SCI or cases with incomplete palsy.

Key words: Spinal cord injury, Voxel-based morphometry, Anatomical change, Brain, Rehabilitation

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The pathological characteristic of spinal cord injury (SCI) is impairment in the neural transmission between the brain and any site below the injury site of the spinal cord through interruption in afferent and efferent fibers[1]. In recent years, studies on SCI using animal models and humans reported that atrophic neuronal changes in the sensory-motor system could occur, in addition to the spinal cord, in brain regions without lesions[2-7]. Meanwhile, neural restructuring was shown to occur in the cortical area in association with the recovery of motility through rehabilitation following SCI[8,9].

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Voxel-based morphometry (VBM) is one of the ways to investigate non-invasively anatomical changes in the human brain[10]. Several studies have been reported that used VBM to investigate anatomical changes in the gray matter (GM) and white matter (WM) following SCI[11-17]. However, the results varied considerably between them. One study reported that no atrophic change was noted in gray matter volume (GMV) in the primary motor area, which is responsible for movement[16], while other studies reported that the GMV decreased significantly compared to that in healthy control individuals[11-15,17], and no consensus has been reached. The variation in these results may be due to differences in the selection of study participants in terms of site of SCI, time from the injury, injury type (traumatic or non-traumatic), and complete or incomplete injury.

VBM analysis results indicated the degree of motility recovery and associated areas[12,15]. Anatomical changes in the brain may be used as a biomarker for the prognosis of

Table 1. Characteristics of individuals with spinal cord injury.

ID	Age (years)	Gender	Time since injury (days)	Level of lesion	AIS classification
1	24	M	181	Th11	A
2	21	M	184	Th10	A
3	43	M	252	Th5	A
4	63	F	301	Th2	A
5	52	M	180	Th4	A
6	51	M	298	Th9	A
7	20	F	225	Th11	A
8	54	M	229	Th10	A
9	35	M	244	Th5	A
10	45	M	201	Th7	A
11	53	F	282	Th8	A
12	60	M	192	Th10	A
Mean±SD	43±14		231±43		

Gender; M = male; F = female. Level of lesion; Th = thoracic level SCI. AIS classification A; complete - no sensory or motor function is preserved in sacral segments S4-S5. SD = standard deviation

motility recovery following SCI and the development of rehabilitation therapy. Adjusting selection criteria for study participants and investigating morphological changes in the brain following SCI is a study of high clinical significance.

The aim of this study is to investigate morphological changes in the brain of individuals in the chronic complete traumatic thoracic spinal cord injury (ThSCI) using VBM. A notable study on the chronic complete ThSCI using VBM was reported by Wrigle et al.[12], which revealed volume reduction in the primary motor cortex and cognitive regions (temporal cortex, anterior cingulate cortex, prefrontal cortex, etc.) compared to those in healthy control individuals. However, their report only investigated areas with reduced volume and no results for areas with increased volume were shown. ThSCI undergoes dynamic physical changes in a manner related to activities of daily living. Therefore, we investigated not only the atrophic region of the brain volume but also the region which showed increased brain volume.

Methods

Participants

Twelve individuals with chronic traumatic complete ThSCI [mean (SD) age was 43 (14) years, range 21 - 63 years, 3 females] were recruited for this study from the Chiba Rehabilitation Center (Chiba, Japan), who fulfilled the following inclusive criteria, over 6 months onset injury, clinically lower limb motor complete, no head or brain region, no seizure, no medial or mental illness, no contraindications (Table 1). Twelve healthy participants participated in the control group [mean (SD) age was 38 (12) years, range 22 - 61 years, 3 females]. Their median age was not significantly different from ThSCI individuals (Mann-Whitney U test, p = 0.01). They had no neurological disease or history of psychiatric diseases. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Ethics Commission of Chiba Rehabilitation Center, Japan (Approval number: Medical 30-12). Written informed consent was obtained from all participants.

MRI acquisition

All participants were scanned on a 3T MRI scanner (Magneton Skyra, Siemens Medical Solutions, Erlangen, Germany) operated with a radio frequency body transmit and a 32-channel birdcage head coil. Sagittal high-resolution 3D T1-weighted anatomical images were acquired using a magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence with the following parameters: repetition time (TR) = 2,700 ms, echo time (TE) = 2.33 ms, flip angle (FA) = 7°, slice thickness = 1.0 mm with no gap, matrix size = 256 × 256, field of view (FOV) = 256 mm × 256 mm. The acquisition time was approximately 5 min for this sequence.

VBM data analysis

VBM analysis was processed using SPM12 (Statistical Parametric Mapping, http://www.fil.ion.ucl.ac.uk/), compiled with the MATLAB version R2014a (MathWorks, Natick, MA, United States) with the VBM module. First, every scan was aligned to the anterior commissure manually. T1-weighted MR images were segmented into gray matter, white matter, cerebrospinal fluid, bone, soft tissue, and air/background after bias regularization. Images of gray matter and white matter were spatially normalized to the Montreal Neurological Institute (MNI) space through diffeomorphic anatomical registration through exponentiated lie algebra (DARTEL) algorithm[18,19]. The total amount of GMV and white matter volume (WMV) of each voxel was

obtained through modulation. Additionally, the resulting GM and WM images were smoothed with a Gaussian kernel with a full width at half maximum (FWHM) of 8 mm. Finally, the total GMV and WMV was calculated based on the modulated images and total intracranial volume (TIV) was calculated as the sum of GMV and WMV.

VBM statistical analysis

GMV and WMV alterations were assessed by comparing SCI with controls, using the standard general linear model (GLM) implementation in SPM12 for independent two-sample t-tests. Age, gender, and TIV were modeled as covariates of no interest. Statistical parametric maps of two different contrasts (Controls > SCI and SCI > Controls) were created by applying a significant threshold of $p < 0.001$ (uncorrected) and a cluster size of 10 voxels.

Results

We have conducted a whole-brain voxel-based analysis of GMV and WMV in healthy control individuals and individuals with ThSCI by using the VBM approach. Compared with healthy controls, individuals with ThSCI had significantly decreased regional GMV in the right paracentral lobe (PCL), left dorsal premotor cortex (PMd), right superior temporal gyrus (STG), left middle frontal gyrus (MFG), left superior parietal lobe (SPL), left amygdala, right parahippocampus, and lower WMV in the right subcortical PCL (Table 2, Fig. 1).

On the other hand, compared to healthy controls, individuals with ThSCI had significantly increased regional GMV in the left primary sensorimotor cortex (SM1), and right precuneus. Furthermore, they had significantly increased regional WMV in the left posterior limb of the internal capsule (ICpost) and right subcortical occipital lobe (OCL) (Table 3, Fig. 2).

Discussion

As we compared changes in the cerebral structure of chronic phase ThSCI cases with healthy control individuals, we revealed volume reduction in regions associated with sensory/motor functions such as right PCL — the primary SM1 for lower limbs, left PMd, and left SPL. Additionally, significant volume reduction was observed in cognitive areas such as the right STG, left amygdala, and right parahippocampal gyrus. Furthermore, several regions with increased volume were noted in the ThSCI group.

Individuals with SCI lose motor or sensory functions below the level of the injury site due to degeneration of afferent and efferent motor fibers[1]. Moreover, studies have reported that motor command signals from the brain as well as sensory feedback from the periphery are blocked in the SCI site, causing functional and structural alterations in the brain[20-22]. In the VBM of the brain, GMV reflects atrophic or increasing changes in functional localization, while WM reflects changes in projective fibers, such as the corticospinal tract and associative fibers.

Several studies reported changes in GMV in the brain of individuals with SCI[11-17], demonstrating volume reduction mainly in the primary motor cortex (M1) and primary and secondary somatosensory cortex. Among these studies, a study on complete ThSCI using VBM[12] revealed volume reduction in the SM1 for lower limbs, and similar results were obtained in the present study, in which volume reduction occurred in the same area. Similarly, studies on individuals with hemiplegia following subcortical stroke[23,24] reported GMV reduction in the SM1 in the injured hemisphere. Anatomical change is believed to occur in the motor region of the brain because of long-term non-use and incompetence of paralyzed limbs following the disease onset. In our study, the non-use of lower limbs by participants, due to paralysis in lower limbs following ThSCI, was associated with reduced GMV in PCL. Similarly, the reduced WMV in the subcortical area of the right PCL is considered to be a result of the decline in fibers that project signals from the PCL, according to the same mechanism as GMV.

With regard to sensory/motor regions, GMV reduction was noted in the PMd and SPL. The PMd is a higher motor area associated with motor preparation, which has been demonstrated to function with the M1 during voluntary movement and represents the somatotopy of lower limbs[25-27]. Loss of motility in lower limbs is thought to have resulted in the volume reduction in the area corresponding to lower limbs in PMd. In addition, SPL is a higher somatosensory area and it can be inferred that loss of input into the primary sensory region associated with the interruption of afferent fibers caused GMV reduction in the same region as a secondary phenomenon.

In the present study, volume reduction was also observed in cognitive regions. Previous studies reported GMV decline in the prefrontal cortex and limbic system, including anterior cingulate cortex, STG, and amygdala[12,15]. Likewise in this study, the volume decline was observed in nearly the same regions. Although change in the emotional aspect following SCI may have contributed to the volume reduction, it is not clear the extent to which the cognitive psychological function contributes to the volume reduction. As areas correlated with the recovery of lower limb motility in incomplete cervical SCI, Villiger et al.[15] reported to have observed positive correlations between the improvement of lower extremity motor score of American Spinal Injury Association impairment scale (LEMS) and GMV in the temporal lobe, hippocampus, and between improvement of Berg balance scale (BBS) and GMV in the temporal lobe. Participants in our study were cases with complete loss of lower limb function and, in agreement with the study of Villiger et al.[15], reduction in GMV was noted in the tempo-

Table 2. Gray matter and white matter volume decreases (e.g., atrophy) at whole brain between individuals with spinal cord injury and healthy control individuals.

Anatomical region	Peak MNI coordinates			Cluster size (voxels)	Peak T-value
	X	Y	Z		
Gray matter					
Paracentral lobe (R)	9	-35	66	26	4.46
Dorsal premotor cortex (L)	-36	-8	65	82	5.38
Superior temporal gyrus (R)	66	-3	-3	429	5.28
Middle frontal gyrus (L)	-47	38	27	32	4.85
Superior parietal lobe (L)	-29	-53	57	39	3.69
Amygdala (L)	18	-2	-14	32	3.28
Parahippocampus (R)	15	0	-18	22	4.33
White matter					
Subcortical paracentral lobe (R)	12	-35	72	20	4.17

MNI = Montreal Neurological Institute

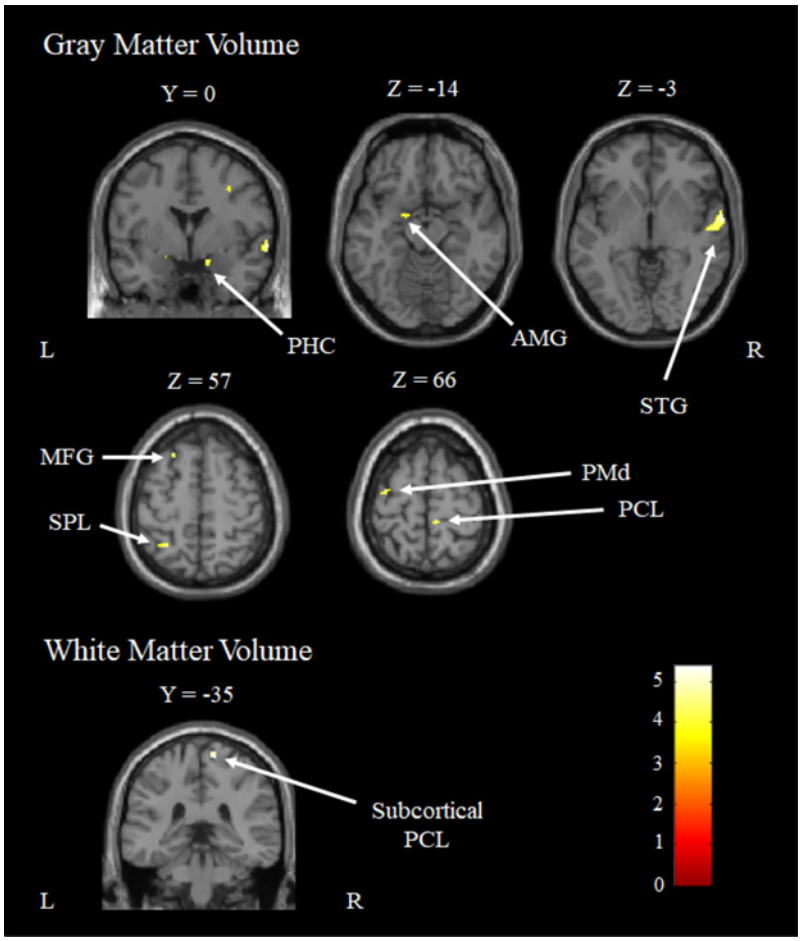

Fig. 1 Statistical parametric maps ($p < 0.001$, uncorrected and a cluster size of 10 voxels) showing regions of gray matter and white matter volume decreased in participants with ThSCI compared with healthy control participants. The location of each slice in Montreal Neurological Institute space is shown at the above of each section. Abbreviations: L, left; R, right; PHC, parahippocampus; AMG, amygdala; STG, superior temporal gyrus; MFG, middle frontal gyrus; SPL, superior temporal gyrus; PMd, dorsal premotor cortex; PCL, Paracentral lobe.

Table 3. Gray matter and white matter volume increases at whole brain between individuals with spinal cord injury and healthy control individuals.

Anatomical region	Peak MNI coordinates			Cluster size (voxels)	Peak T-value
	X	Y	Z		
Gray matter					
Primary sensorimotor cortex (L)	-30	-28	52	26	5.72
Precuneus (R)	8	-48	65	20	3.44
White matter					
Posterior limb of the internal capsule (L)	-24	-33	12	84	4.61
Subcortical occipital lobe (R)	11	-76	14	15	4.40

MNI = Montreal Neurological Institute

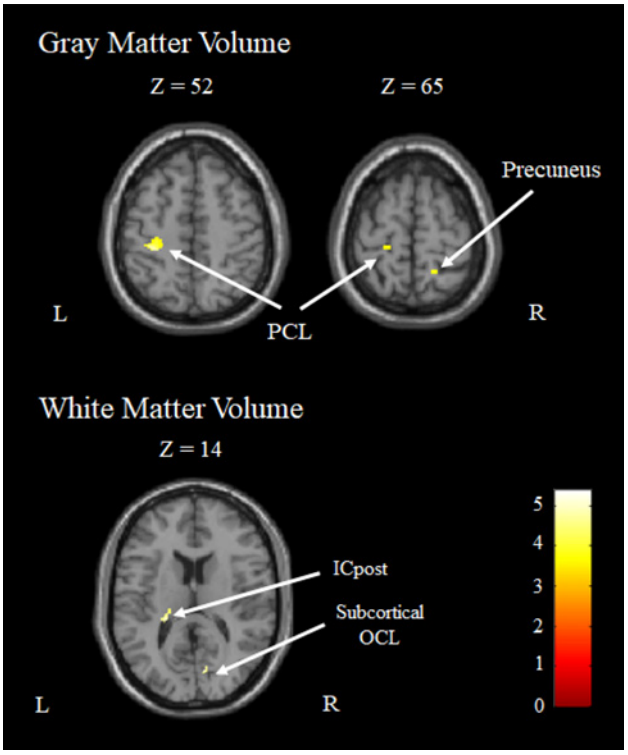

Fig. 2 Statistical parametric maps ($p < 0.001$, uncorrected and a cluster size of 10 voxels) showing regions of gray matter and white matter volume increased in participants with ThSCI compared with healthy control participants. The location of each slice in Montreal Neurological Institute space is shown at the above of each section. Abbreviations: L, left; R, right; PCL, Paracentral lobe; ICpost, posterior limb of the internal capsule; OCL, occipital lobe.

ral lobe and hippocampus. A VBM study of ThSCI also showed atrophy in the temporal lobe[12]. These findings indicate that reduced lower limb motor function causes atrophy of these cognitive areas and further demonstrates that it may be a biomarker for recovery of lower limb function following SCI.

This study examined regions with increased volume in the SCI group. Compared to healthy control individuals, increases in GMV were observed in the left SM1 and right precuneus in the SCI group. As for WM, volume increases were observed in the left ICpost and OCL subcortical region.

Studies on cervical SCI using VBM reported volume decline in the SM1[11,13,14]. On the other hand, there was a volume increase in the left SM1 in this study. It is surmised that volume increases occur in the areas corresponding to fingers and arms in the somatotopy of the SM1. Furthermore, performing task-oriented training that actively use the hemiparetic upper limb in stroke rehabilitation increased GMV in the SM1 in the injured hemisphere[28]. This demonstrated that increased use of the hemiparetic upper limb increased the brain area corresponding to the usage site. Participants in this study were with ThSCI complete palsy and their upper limb functions were normal. Individuals with ThSCI change their mode of conduct in a way that life activities, such as transfer and wheelchair driving, can be performed with upper limbs only. Compared to healthy people or those before injury, situations where use of upper limbs is required have necessarily become more prominent and overuse of upper limbs is thought to have resulted in the increase in GMV of the left SM1. In addition, an increase in WMV was observed in the left ICpost where the corticospinal tract passes through and this is considered to be the result of a similar mechanism as to the one that caused an increase in GMV in the left SM1.

Volume increases were also noted in sensory regions, such as the precuneus and the OCL subcortical region. Since individuals with complete ThSCI have dynamic changes in the sensory input system associated with loss of somatosensory functions below the level of injury, a new body image must be established. Since the OCL is the visual region and the precuneus is considered as a region that constitutes the somatotopic map[29], it is speculated that to obtain a new body image, these functions compensated the loss of somatic sensation and contributed to the volume increase in both of these regions. The increased gray matter volume in both regions has also been indicated in stroke in VBM studies on both humans[30,31], and animal models[32].

In the present study, we observed several regions that increased or decreased asymmetrically. Because of the laterality of the left and right hemispheres in brain function, contrasting changes are not always observed. However, it is reasonable to expect a bilateral appearance in areas such as the primary motor cortex. We believe that clear results can be obtained in a study with a large sample size.

The results of the present study also demonstrated the presence of areas with increased volume in addition to areas with decreased volume in association with ThSCI-induced changes in physical function. Several limitations of this study should be noted. First, the sample size was relatively small, and the statistical power ($p < 0.001$, uncorrected) is therefore low. However, the areas that were reduced in this study showed similar results to previous VBM studies in SCI, and we are confident that the findings show differences from healthy subjects. Indeed, this assumption should be verified in the future with larger sample sizes. It is predicted that the affected brains areas that differ between individuals with SCI and healthy individuals will become clearer by increasing the number of cases. Moreover, to reveal changes in the brain structure following SCI, it is necessary to compare ThSCI patients with those who have sustained cervical spinal cord injuries and patients with incomplete injury, and to conduct a longitudinal study in the same group. Clarification of the relationship between changes in the brain structure and residual disabilities may be used to determine the rehabilitation effect.

Conflict of Interest: The authors declare no conflict of interest.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Self-rated Changes of Health Status during Stay-at-home Orders among Older Adults Using the Long-term Care Insurance System of Japan: A Cross-sectional Study

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ABSTRACT. Objectives: To reveal self-rated changes of health status during stay-at-home orders among older adults and to verify whether decrease in frequency of going outdoors during these orders was related to self-rated changes in health status.

Method: A self-completed questionnaire for older adults was provided in 2 dayservice facilities and a nursing station. We operationally defined health status with 4 domains (motor function, oral and swallowing function, depression, and social networks) and designed the questionnaire to determine self-rated changes in health status using factor analysis. After factor analysis, regression analyses were conducted.

Dependent variable was each factor score (self-rated changes of health status), and independent variable was decrease in frequency of going outdoors.

Results: Approximately 80% of participants answered that their health status had "worsened" in motor function (75.0%-87.2%). Moreover, more than 70% of participants answered "worsened" in "Feeling energy" and "Getting together and speaking with friends" (72.3% and 75.7%, respectively). Regression analyses demonstrated that, after adjusting for covariates, the decrease in frequency of going outdoors was related to self-rated changes of motor function and friend network.

Conclusion: During stay-at-home orders, older adults felt deterioration in their motor function, in feeling energy, and in their friend network, especially people who had decreased their frequency of going outdoors felt more deterioration in their motor function and in their friend network.

Key words: COVID-19, Frequency of going outdoors, Self-rated health, Stay-at-home orders

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A new type of coronavirus disease called COVID-19 have been widespread around the world. The World Health Organization declared a state of emergency on January 31 2020. Since then, in order to prevent the spread of COVID-19, many countries around the world legislated or recommended stay-at-home orders, or "lockdowns," which have resulted in individual and collective restrictions on participating in outdoor activities.

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At the end of February 2020, the Japanese government requested that people reduce their attendance at sports and cultural events. On March 26, in 4 prefectures, including Tokyo, governors requested that residents stay at home and avoid non-essential trips outdoors. On April 7, the Japanese government declared a state of emergency and requested residents in 7 prefectures, including Tokyo, avoid unnecessary or non-urgent visits outdoors until the state of emergency was lifted (this was called stay-at-home orders, or "gaisyutsu-jisyuku-yosei" in Japanese.) On May 4, the stay-at-home declaration was extended until May 25, meaning that residents must remain at home for approximately 2 months.

Research has shown that going outdoors is related to various indicators of health status among older adults. Cross-sectional studies of older adults revealed that those

who went outdoors infrequently was more likely to have mobility impairments[1,2], limitation in activities of daily living (ADLs)[1-3], limitation in instrumental activities of daily living(IADLs)[1-3], cognitive decline[1,2,4], depressive mood[1,2,5], less social participation[1], low oral function[1], low meal intake[6], low health rerated quality of life[7], and so on. Moreover, several prospective cohort studies of older adults showed that frequency of going outdoors was related to differences in mortality[5], mobility[8], ADLs[9], IADLs[5,8,10], and self-rated health[9]. Thus, going outdoors is an important factor for health status.

Stay-at-home orders, namely social or collective restrictions on outdoor activities have been unprecedented in recent years. A Scoping Review including 41 articles showed physical activities (PA) significantly decreased regardless of the population studied[11], and in Japan, a cross-sectional online survey among older adults also clarified PA during stay-at-home orders significantly decreased compared to PA before stay-at-home orders[12]. Moreover, several studies demonstrated decrease PA during COVID-19 pandemic was related to higher level of depression[13,14].

In the same way as PA, stay-at-home orders might decrease frequency of going outdoors among older adults, which might lead to a decline in their health status. Therefore, it was necessary to study how health status might have changed during stay-at-home orders and to verify whether decrease in frequency of going outdoors due to the stay-at-home orders was related to health status, as previous studies[1-10] conducted in non-pandemic conditions showed that relationship.

Health status is measured both subjectively (self-rated health) and objectively; self-rated health has a predictive value for mortality equivalent to objectively measured health[15]. Although, in general, objectively measured health is more reliable, to better understand the needs of older adults, it is also important to focus on their own subjective perspectives about changes in their health status.

The objectives of this study were to reveal self-rated change in health status among older adults during stay-at-home orders and to verify whether decrease in frequency of going outdoors during stay-at-home orders were related to self-rated change in health status.

Method

Procedure and participants

This cross-sectional study was done with questionnaires completed by older adults using the long-term care insurance system of Japan. The survey was conducted in 2 day-service facilities and a nursing station in Setagaya Ward, Tokyo, from May 11 to May 31, 2020. We defined stay-at-home as staying at home because of social or collective restrictions on outdoor activities that is not attributed to personal factors. Moreover, during stay-at-home and before stay-at-home were defined as periods in April and May 2020 and in January and February 2020, respectively.

During the survey period, 262 people were registered in the above-listed places. Exclusion criteria was people with diagnosis of dementia or cognitive deficits who had no family to represent them in answering questionnaire. We searched those with diagnosis of dementia or cognitive deficits in medial or care record and ask medical or care staffs if they have family to represent them in answering. Consequently, 11 people were excluded, and we sent questionnaire to 251 people. Informed consent was obtained from all participants or their family members. We confirmed provisions of the Declaration of Helsinki, and this study was approved by the ethical committee in the Arakawa campus of Tokyo Metropolitan University (approval number: 20016).

Measurements

Participant characteristics

We collected participant characteristics of age, sex, and living alone in the questionnaire. The level of care in the long-term care insurance system of Japan[16], and disease information were collected from medical or care records. We investigated if each participant had the following diseases or conditions: orthopedic disease, stroke, neurodegenerative diseases (e.g. Parkinson's diseases, not including dementia), spinal cord injury, peripheral nerve disease, heart disease, pulmonary disease, kidney disease, digestive disease, psychiatric diseases (except for dementia), cancer, dementia, diabetes mellitus, and other diseases. We defined sum of disease domain as degree of multi-morbidity (e.g., if a participant had knee arthritis and stroke, the degree of multi-morbidity was defined as 2).

Going outdoors

We defined going outdoors as follows, with minor modification to Fujita's definition[1]: going outdoors was going out from the house with or without a caregiver and includes shopping, taking a walk, going to a doctor or day service facility, and going for leisure activities; it excludes outdoor gardening or taking out the garbage.

In the questionnaire, we investigated frequency of going outdoors and destinations or purposes for going outdoors "before stay-at-home" and "during stay-at-home." Our survey was conducted in May 2020. Therefore, "during stay-at-home" data were collected at that time, whereas the "before stay-at-home" data were recalled from participant memory. For frequency, we set 7 options (1: never go outdoors, 2: go outdoors once a month, 3: once in 2 weeks, 4: once a week, 5: 2-3 times a week, 6: 4-6 times a week, 7: everyday). If the frequency of going outdoors during the stay-at-home orders was lower than the frequency before the stay-at-home orders, that was defined as a "decrease."

For destination or purposes, we set 11 options (walking, going to the hospital, going to day-services, shopping, visiting friends, visiting family, doing leisure activities, doing intellectual activities, participating in club activities, volunteering, or other).

Self-rated changes in health status

We operationally defined health status in 4 domains: (1) motor function, (2) oral and swallowing function, (3) depressive mood, and (4) social networks. We designed the questionnaire with 24 questions from these domains. For motor function, we defined 6 construction concepts (muscle strength of lower limb, muscle strength of upper limb, body flexibility, balance ability, gait ability, and endurance) and set content for each concept. For swallowing and oral function, depressive mood, and social networks, we defined construction concepts using constructs and question contents from existing scales: questionnaire to screen dysphagia[17], Geriatric Depression Scale 15[18], and Lubben Social Network Scale[19], respectively. All content was designed to detect worsening health status, with 4 ordinal options (0: never worsened, 1: not worsened, 2: somewhat worsened, and 3: much worsened). See Appendix 1 for question contents.

Statistical analysis

We analyzed data with SPSS var. 26 for Mac (IBM Japan), and the level of statistical significance was defined as $p < 0.05$.

To verify whether construct of self-rated changes of health status corresponded with predetermined domains, we conducted factor analysis. Method of factor extraction was least squares solution, and method of rotation was varimax rotation. The contents for each factor were determined by criteria that factor loadings were greater than 0.4 or smaller than -0.4. If an item was related to 2 or more factors, we considered bigger factor loadings in the item. After factors were determined, factor scores for each case were calculated in each factor. Higher factor scores indicated worsening health status.

To verify decrease in frequency of going outdoors during stay-at-home orders was related to self-rated change in health status, regression analyses were conducted for each factor score. The dependent variable for each regression analysis was each factor score. First, we checked whether each factor score was normally distributed using the Shapiro-Wilk test, and 3 out of 5 factor score did not normally distributed. Therefore, we converted all factor score (a continuous variable) into a dichotomous variable (0: under 50 percentile, 1: more than 50 percentile) and conducted multiple logistic regression analysis. Independent variable was decrease in frequency of going outdoors and covariates were age, sex, living alone, level of care needs, degree of multi-morbidity, and frequency of going outdoors before the stay-at-home orders.

Table 1. Participants Demographics (N = 148)

Age, mean (SD)	81.4 (7.6)
Sex, n (%)	
Male	67 (45.3)
Female	81 (54.7)
Living alone, n (%)	36 (24.3)
Decrease in frequency of going outdoors, n (%)	52 (35.1)
Level of care needs, n (%)	
Not-eligible	3 (2.0)
Need-support-1	30 (20.3)
Need-support-2	30 (20.3)
Level-1	33 (22.3)
Level-2	31 (20.9)
Level-3	13 (8.8)
Level-4	6 (4.1)
Level-5	2 (1.4)
Disease, n (%)	
Orthopedics / musculoskeletal disease	78 (52.7)
Stroke	41 (27.7)
Neurodegenerative disease except for dementia	20 (13.5)
Spinal cord injury	2 (1.4)
Peripheral nerve disease	7 (4.7)
Heart disease	24 (16.2)
Pulmonary disease	11 (7.4)
Kidney disease	9 (6.1)
Digestive disease	5 (3.4)
Psychiatric disease	6 (4.1)
Dementia	7 (4.7)
Cancer	12 (8.1)
Diabetes mellitus	19 (12.8)
Other diseases	14 (9.5)
Degree of multimorbidity, median (min-max)	2 (1-5)

SD: standard deviation

Results

A total of 193 people responded to the questionnaire. After excluding those who did not permit us to collect data from their own medical or care records (n = 6), those who had missing values (n = 26), and those who were younger than 65 years (n = 13), 148 participants were included in this study.

Participant characteristics were shown in Table 1. People who decreased frequency of going outdoors were 35.1%. Going outdoors for walking, shopping, attending day services, and going to the hospital were likely to continue during the stay-at-home orders (proportion of interruption: 14.6%-34.2%), whereas going outdoors to visit friends or family, doing leisure activities, doing intellectual activities, attending club activities, and volunteering tended to be interrupted (proportion of interruption: 64.3%-

Table 2. Question content and results of Factor Analysis

content	1st factor	2nd factor	3rd factor	4th factor	5th factor
Muscle strength of lower limb	**.812**	.157	.059	.072	.104
Muscle strength of upper limb	**.740**	.221	.178	.013	.028
Body flexibility	**.727**	.238	.168	.154	.064
Balance ability	**.768**	.159	.206	.223	.081
Gait ability	**.730**	-.022	.255	.114	.133
Endurance	**.768**	.133	.188	.119	.118
Difficulty to drink fluids	.227	.230	**.674**	.000	.010
Choking while eating	.142	.063	**.842**	.026	.037
Choking while drinking liquids	.161	.060	**.736**	.171	.063
Difficulty to eat hard foods	.354	.284	.358	-.119	.150
Food falls out of the mouth	.192	.035	**.543**	.173	.293
Food to be left in the mouth	.135	.167	**.542**	.077	.102
Satisfaction with life	.165	**.766**	.132	.171	.184
Feeling happy	.161	**.713**	.110	.194	.120
Feeling helpless	.257	**.571**	.159	.257	.012
Feeling worthless	.076	**.561**	.032	.188	.099
Being bored	.066	**.564**	.152	.137	.128
Feeling energy	.357	**.549**	.183	.143	.296
Getting together and speaking with friends	.186	.238	.167	.139	**.629**
Speaking with friends about private life	.133	.338	.154	.169	**.795**
Asking friends for help	.115	.133	.252	.382	.217
Getting together and speaking with family	.143	.302	.107	**.653**	.061
Speaking with family about private life	.108	.440	.039	**.728**	.204
Asking family for help	.135	.201	.058	**.792**	.050
variance explained (VE)	4.10	3.21	2.87	2.17	1.46
proportion of VE [%]	17.1	13.4	12.0	9.0	6.1
cumulative proportion of VE[%]	17.1	30.5	42.4	51.5	57.6
Cronbach α	0.91	0.85	0.83	0.85	0.79

85.7%).

In self-rated changes of health status, in 6 contents related to motor function, approximately 80% of participants answered "worsened" (75.0%-87.2%), whereas fewer participants answered "worsened" for 6 contents related to oral and swallowing function (20.9%-50.7%). In contents related to depressive mood and social networks, 72.3% of participants answered "worsened" in "Feeling energy," and 75.7% answered "worsened" in "Getting together and speaking with friends." More detail results were shown in Appendix 2.

While we had defined health status in 4 domains before analysis, factor analysis extracted 5 factors and the cumulative proportion of variance explained was 57.6% (See Table 2). We named these factors as follows: 1st factor: "motor function," 2nd factor: "depressive mood." 3rd factor: "oral and swallowing function," 4th factor: "family network," and 5th factor: "friend network."

Results of the multiple logistic regression analyses are shown in Tables 3. Decrease in the frequency of going outdoors was related to the 1st factor score (OR 2.16, 95%CI 1.04-4.47) and the 5th factor score (OR 2.22, 95%CI 1.08-4.59).

Discussion

Our study revealed self-rated changes of health status during stay-at-home orders among older adults using the long-term care insurance system of Japan. In the questionnaire, many participants answered "worsened" in motor function, feeling energy, and getting together and speaking with friends. During stay-at-home orders, in addition to restrictions for going outdoors, people were requested to keep "social distancing, or staying 2 meter (6 feet) apart". Moreover, the fear of infection of COVID-19 expanded among people. These conditions forced people to alter their behavior and changed their environments, which might lead older adults to feel deteriorations in motor function, depressive mood, and friend network.

However, participants in this study were recruited from 2 day-service facilities and a nursing station, and these placed emphasis on rehabilitation services. Therefore, the participants in this study might be concerned with their motor function and thus sensitive to tiny changes therein,

Table 3. Results of multiple regression analysis for factor scores

Independent variable and covariates	1st factor score	2nd factor score	3rd factor score	4th factor score	5th factor score
Decrease in frequency of going outdoors [decrease: 1]	**2.16 (1.04-4.47)**	1.18 (0.05-2.41)	1.01 (0.05-2.03)	0.87 (0.43-1.73)	**2.22 (1.08-4.59)**
Age†	**1.05 (1.00-1.11)**	0.99 (0.94-1.03)	0.99 (0.94-1.03)	0.98 (0.94-1.03)	1.02 (0.97-1.06)
Sex [female: 1] †	0.87 (0.42-1.84)	2.05 (0.99-4.24)	0.97 (0.47-1.97)	0.73 (0.36-1.49)	0.40 (0.19-0.85)
Care need level†	**0.78 (0.61-1.00)**	0.82 (0.64-1.05)	1.15 (0.91-1.46)	0.87 (0.69-1.09)	0.89 (0.70-1.13)
Living alone [alone: 1] †	1.20 (0.52-2.75)	1.28 (0.57-2.92)	0.48 (0.21-1.09)	1.33 (0.60-2.95)	0.86 (0.38-1.95)
Degree of multimorbidity†	**1.58 (1.00-2.51)**	0.78 (0.50-1.21)	0.92 (0.61-1.41)	1.09 (0.71-1.66)	0.73 (0.47-1.13)
Frequency of going outdoors before stay-at-home†	0.89 (0.66-1.20)	0.93 (0.69-1.24)	0.93 (0.70-1.24)	1.02 (0.77-1.73)	1.10 (0.82-1.48)

Values in this Table mean Odds ratio (95% confident interval).

1st to 5th factor scores were indicators of motor function, depressive mood, oral and swallowing function, family network and friend network, respectively and they were converted into dichotomous values (0: under 50 percentile, 1: more than 50 percentile), which value "1" indicated greater deterioration of health status.†: Covariates

Bold letters: $p < 0.05$

which means the participants might overestimate the changes in their motor function.

Multiple logistic regression analyses revealed that decrease in the frequency of going outdoors was related to self-rated changes in motor function and friend network. Previous studies showed that lower frequency of going outdoors led to impairments in mobility[8], ADLs[9], and IADLs[5,8,10]. Moreover, lower frequency of going outdoors was also related to poor social networks[1]. Although outcomes in this study were not equal to those in previous studies, the results of present study corresponded with those of the previous studies. Decrease in frequency of going outdoors might causes lower amounts of physical activities and fewer opportunities to meet with friends, which can lead to feeling deterioration in motor function and friend network. Although this self-rated deterioration in motor function and friend network shown in this study did not necessarily indicate real changes of them, in pandemic, supports for older adults to help maintain their motor function and friend network might be needed.

Previous studies found that lower frequency of going outdoors was related to depression[1,2,5], whereas this current study demonstrated no relationship between decrease in frequency of going outdoors and change of depressive mood. This finding might have occurred because of differences in the contexts where each study was conducted. Our current study was conducted during an infectious disease pandemic and subsequent stay-at-home orders, which meant that other factors might be more related to depressive mood.

While previous studies found that lower frequency of going outdoors was related to oral function[1] and reduction of meal intake[6], and we hypothesized that a decrease in frequency of going outdoors causes a reduction of meal intake and that leads to a decrease in oral and swallowing function, no relationship existed between decrease in frequency of going outdoors and self-rated change of oral and swallowing function. Decrease in frequency of going outdoors might indirectly lead to deterioration in oral and swallowing function because of a reduction in meal intake, which means stay-at-home for 2 months might be insufficient to lead to a decrease in oral and swallowing function.

Decrease in frequency of going outdoors was not related to deterioration in family network. Many participants in this study lived with family members. Moreover, their families might have visited them because Japanese government did not prohibit them from visiting in necessary or urgent situations. Therefore, even If the participants decreased their frequency of going outdoors, contact with the family network was likely to be maintained.

The present study had several limitations. First, among approximately 85% of participants in this study, care needs were not greater than Level 2. A statistical report of long-term care insurance system in May 2020 showed that the proportion of those who have a Need-Support-1 to Level-2 certification was 65.5%[20], meaning that participants in this study were biased for those with mild or moderate impairments. Therefore, results of present study should not be adapted for people with more severe impairments (i.e., Level-3 to Level-5). Second, changes in health status in this study were self-rated and we asked participants whether their health status worsened. This situation might lead them answer "worsened". Moreover, as mentioned above, participants in this study might overestimate the changes in their motor function. Therefore, it is needed to consider changes in health status in this study, especially, motor function might be biased. Further research based on objective data are needed, especially for change in motor function. Third, a previous study has shown a misclassification in the frequency of going outdoors[8]. Moreover, variables of going outdoors before the stay-at-home orders were based

on participants' recall. Thus, misclassification should be also considered in results of this study.

Conclusion

During stay-at-home orders, older adults felt deterioration in their motor function, in their feeling energy, and in their friend network, especially those adults who decreased the frequency of going outdoors felt more deterioration in their motor function and in their friend network.

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Conflict of Interest: The authors declare no conflict of interest.

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Supplementary material (Appendix):
1. Appendix 1. Questionnaire for self-rated changes in health status
2. Appendix 2. Answer for self-rated changes of health status in stay-at-home orders

Appendix 1. Questionnaire for self-rated changes in health status

Construction concept	Content
Muscle strength of lower limb	Recently, have you felt that the muscle strength of your lower limbs and lower back has decreased?
Muscle strength of upper limb	Recently, have you felt that the muscle strength of your upper limbs has decreased?
Body flexibility	Recently, have you felt that your body has felt stiff?
Balance ability	Recently, have you felt that your balance has worsened?
Gait ability	Recently, have you felt that you walk more slowly?
Endurance	Recently, have you felt that you have trouble moving around for long periods of time?
Swallowing function	Recently, have you felt that it is difficult to drink fluids? Recently, have you felt like you have been choking while eating? Recently, have you felt like you have been choking while drinking liquids?
Oral function	Recently, have you felt that it is difficult to eat hard foods? Recently, have you noticed that food falls out of your mouth? Recently, have you noticed that more food seems to be left in your mouth when eating?
Pessimistic mood	Recently, have you felt a decreased level of satisfaction with your daily life? Recently, have you felt that the time you spend feeling happy has decreased?
Negative self-evaluation	Recently, have you felt increasingly helpless? Recently, have you felt increasingly like it is worthless to continue living?
Loss of energy	Recently, have you felt like you are increasingly bored every day? Recently, have you felt a decrease in energy?

Appendix 1. Questionnaire for self-rated changes in health status (Continued)

Friend network	Recently, have you felt that you get together with and speak with friends less frequently?
	Recently, have you felt that you readily speak with friends about your private life less frequently?
	Recently, have you felt that you have asked friends for help less frequently?
Family network	Recently, have you felt that you get together with and speak with family members less frequently?
	Recently, have you felt that you readily speak with family members about your private life less frequently?
	Recently, have you felt that you have asked family members for help less frequently?

All concepts were designed to detect worsening health status, and a 4-item Likert scale was set for each concept (0: never worsened, 1: not worsened, 2: somewhat worsened, and 3: much worsened).

Appendix 2. Answer for self-rated changes of health status in stay-at-home orders

content	much worsened	somewhat worsened	not worsened	Never worsened
	n (%)	n (%)	n (%)	n (%)
Muscle strength of lower limb	67 (45.3)	59 (39.9)	13 (8.8)	9 (6.1)
Muscle strength of upper limb	43 (29.1)	68 (45.9)	26 (17.6)	11 (7.4)
Body flexibility	47 (31.8)	67 (45.3)	28 (18.9)	6 (4.1)
Balance ability	58 (39.2)	71 (48.0)	12 (8.1)	7 (4.7)
Gait ability	82 (55.4)	35 (23.6)	21 (14.2)	10 (6.8)
Endurance	81 (54.7)	47 (31.8)	14 (9.5)	6 (4.1)
Difficulty to drink fluids	6 (4.1)	49 (33.1)	66 (44.6)	27 (18.2)
Choking while eating	7 (4.7)	40 (27.0)	72 (48.6)	29 (19.6)
Choking while drinking liquids	5 (3.4)	38 (25.7)	70 (47.3)	35 (23.6)
Difficulty to eat hard foods	15 (10.1)	60 (40.5)	47 (31.8)	26 (17.6)
Food falls out of the mouth	7 (4.7)	34 (23.0)	72 (48.6)	35 (23.6)
Food to be left in the mouth	5 (3.4)	26 (17.6)	73 (49.3)	44 (29.7)
Satisfaction with life	18 (12.2)	56 (37.8)	59 (39.9)	15 (10.1)
Feeling happy	12 (8.1)	52 (35.1)	60 (40.5)	24 (16.2)
Feeling Helpless	21 (14.2)	67 (45.3)	44 (29.7)	16 (10.8)
Feeling Worthless	7 (4.7)	32 (21.6)	51 (34.5)	58 (39.2)
Being bored	3 (2.0)	34 (23.0)	65 (43.9)	46 (31.1)
Feeling energy	27 (18.2)	80 (54.1)	28 (18.9)	13 (8.8)
Getting together and speaking with friends	46 (31.1)	66 (44.6)	26 (17.6)	10 (6.8)
Speaking with friends about private life	27 (18.2)	56 (37.8)	47 (31.8)	18 (12.2)
Asking friends for help	11 (7.4)	18 (12.2)	85 (57.4)	34 (23.0)
Getting together and speaking with family	20 (13.5)	34 (23.0)	59 (39.9)	35 (23.6)
Speaking with family about private life	6 (4.1)	42 (28.4)	67 (45.3)	33 (22.3)
Asking family for help	9 (6.1)	18 (12.2)	85 (57.4)	36 (24.3)

PHYSICAL THERAPY RESEARCH

CASE STUDIES

The Progress of the Gait Impairment and Brain Activation in a Patient with Post-stroke Hemidystonia

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ABSTRACT. Objective: We explore the effects of body weight-supported (BWS) treadmill training, including the change of cortical activation, on a patient with post-stroke hemidystonia. Patient: The patient was a 71-year-old man with left thalamus hemorrhage. His motor symptoms indicated slight impairment. There was no overactive muscle contraction in the supine, sitting, or standing positions. During his gait, the right initial contact was the forefoot, and his right knee showed an extension thrust pattern. These symptoms suggested that he had post-stroke hemidystonia. Methods: The patient performed BWS treadmill training 14 times over 3 weeks. The effects of the BWS training were assessed by a step-length analysis, electromyography and functional magnetic resonance imaging (fMRI). Results: The patient's nonparetic step length was extended significantly in the Inter-BWS ($p<0.001$) and Post-BWS ($p=0.025$) periods compared to the Pre-BWS session. The excessive muscle activity of the right gastrocnemius medialis in the swing phase was decreased at the Inter-BWS, Post-BWS, and follow-up compared to the Pre-BWS session. The peak timing difference of the bilateral tibialis anterior muscle became significant ($p<0.05$) on the first day of the intervention. The fMRI revealed that the cortical areas activated by the motor task converged through the intervention ($p<0.05$, family-wise error corrected). Conclusion: These results suggest that there was improvement of the patient's symptoms of post-stroke hemidystonia due to changes in the brain activity during voluntary movement after BWS intervention. Body weight-supported treadmill training may thus be an effective treatment for patients with poststroke hemidystonia.

Key words: Post-stroke hemidystonia, Body weight-supported treadmill, Functional magnetic resonance imaging, Electromyography, Step length

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Hemidystonia is a movement disorder that affects the upper or lower half of the body and is caused by abnormal muscle tone. The onset of post-stroke hemidystonia occurs during the chronic stage (range: 3 months to 3 years)[1)]. The most commonly applied treatments for acquired hemidystonia are medication and deep-brain stimulation[1)]. Physical therapy is also sometimes used in patients with acquired hemidystonia, but its benefits are often temporary, and there has been no large-scale double-blind study indicating that physical therapy has sufficient objective benefits to jus-

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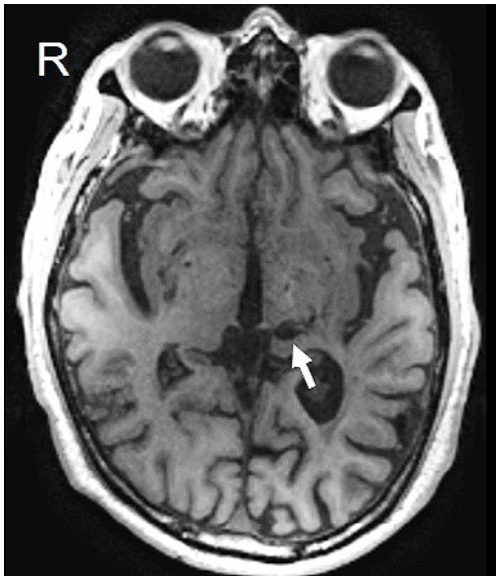

Fig. 1. An MRI T1-weighted image at 13 years after the onset of the patient's cerebral hemorrhage. *White arrow*: The lesion area in the left thalamus.

tify its regular application for acquired hemidystonia. Indeed, systematic reviews have concluded that there is insufficient evidence to recommend any particular strategy for acquired hemidystonia[2-4]. Moreover, an effective intervention for gait disorder in post-stroke hemidystonia patients has not been identified. Case reports of post-stroke hemidystonia patients are thus a valuable resource for information about the success of alternative treatments.

The symptoms of hemidystonia are various. Some hemidystonia patients exhibit obvious symptoms when standing or walking but not at rest[5], suggesting that hemidystonia appears when the patient is bearing his or her body weight. Body weight-supported (BWS) treadmills partially support a patient's body weight by means of an overhead harness, a pelvic belt, and thigh straps, allowing the patient to undergo gait training. Hesse et al.[6] reported that the activity of the soleus muscle was diminished in patients with BWS training compared to those without BWS training. We hypothesized that BWS treadmill training could suppress the symptoms of post-stroke hemidystonia by reducing the weight-bearing burden of patients.

Functional magnetic resonance imaging (fMRI) is a promising modality for revealing the cortical activity of patients with neurological disorders. Two neurophysiological investigations of hemidystonia have been peformed[7,8], and one of these studies revealed abnormal patterns of activity in both the ipsilesional and contralesional hemispheres of hemidystonia patients[8]. We hypothesized that a BWS intervention would normalize the cortical overactivity and alleviate the symptoms of post-stroke hemidystonia. We conducted the present study (1) to explore the effects of BWS treadmill training in a patient with post-stroke hemidystonia by performing a gait pattern analysis and electromyography of the patient's lower extremities, and (2) to investigate the changes in the patient's brain activity after BWS training.

Case Presentation

A 71-year-old Japanese man (height: 175 cm; weight: 63 kg) was admitted to our hospital for rehabilitation. Thirteen years earlier, he had been diagnosed with a cerebral hemorrhage in the left thalamus. At that time, very slight hemiplegia of the right upper and lower limbs was observed, but he could walk without using a brace and could drive a car. Approximately 6 months before his presentation at our hospital, the muscle tone in his right upper and lower limbs increased and he developed an extension thrust pattern[9] that became more pronounced, making it difficult to walk. His chief complaint at that time was that his speed of walking was greatly reduced, making it impossible to travel.

An MRI T1-weighted image is provided in Figure. 1. The patient's awareness was clear, and he had good recognition (Mini-Mental State Examination: 24 points). His motor symptoms showed slight impairment (Fugl-Meyer scores: lower limbs 29/34 points, upper limbs 32/36 points; grip strength: right 15.4 kg, left 34.5 kg). The patella tendon reflex and Achilles tendon reflex of the right side were normal. The patient's range of motion was limited at right knee extension (−10°) and right dorsiflexion (0°). Sensory impairment in the right lower limb was moderate to severe. The patient could walk 100 m without a cane. Regarding activities of daily living (ADLs), his functional level was independent or supervised (functional independence measure: 118 points).

The observation of the patient's dystonia revealed no abnormal movements or postures in the lower extremities, upper extremities, or trunk in the supine, sitting, or standing positions. During his gait, the initial contact of the right leg was the forefoot, and his right knee showed the extension thrust pattern (Fig. 2).

This study was carried out in accord with the Declaration of Helsinki, with approval from the Ethics Committee of the Ibaraki Prefectural University of Health Sciences (approval no. 797). Written informed consent was obtained from the patient for the publication and use of the images accompanying this case report.

Methods

Intervention

The patient underwent BWS treadmill training with a body-weight support system (Unweighing System 945-480; Biodex Medical Systems, Shirley, NY) and a treadmill (Autorunner AR-200; Minato Medical Science Co., Osaka, Japan). He had had no prior experience with treadmill training, including BWS training. To help him maintain a sym-

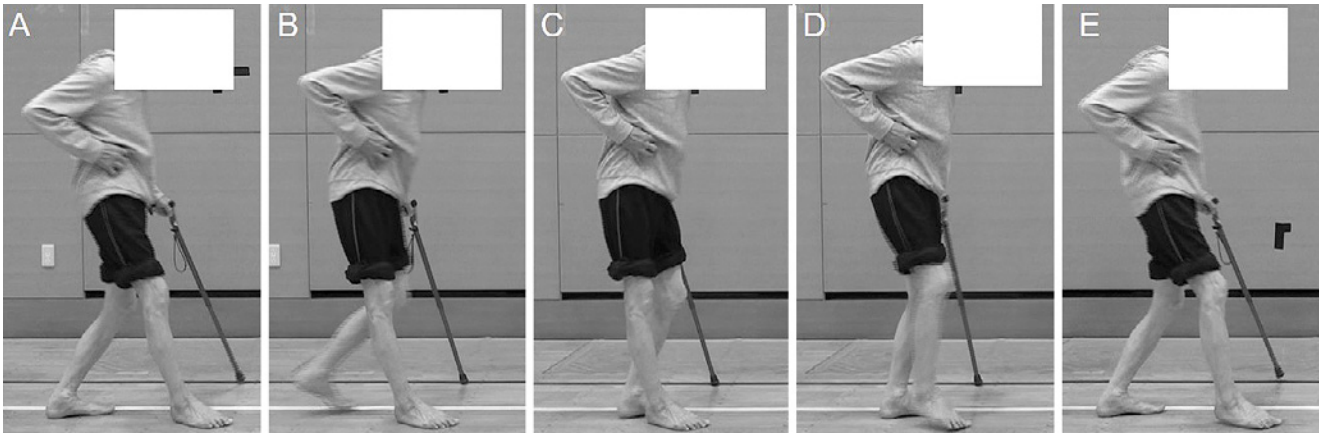

Fig. 2. The patients' gait posture at a gait cycle. **A:** Right initial contact; **B:** Left foot-off; **C:** Left initial contact; **D:** Right foot-off; **E:** Right initial contact. The extension thrust pattern of the right knee was confirmed in panels A to B.

metrical gait pattern as long as possible, we set the following parameters in the first session: (1) body support equal to 20% of his body weight, and (2) gait speed of 0.7-1.2 km/hr. In each BWS session, two skilled physical therapists assisted the patient's leg movements and supported his balance. In the intervention session, no ankle-foot-orthosis (AFO) was used. The patient's fatigue was assessed during the intervention. The BWS was stopped if and when the Borg scale[10] exceeded 13 or when the patient asked to stop due to fatigue.

Timeline

The patient underwent BWS treadmill training sessions 14 times over a 3-week period, for a duration of ≤20 min/session and no more than one session per day. We evaluated both the immediate and long-term effects of the BWS training. To determine the immediate effect of BWS training in this patient, we performed three evaluations on the first day of the intervention—namely, a step-length analysis and electromyography (EMG) assessment before (Pre-BWS), during (Inter-BWS), and after (Post-BWS) the BWS training.

Before starting the BWS treadmill training, the patient performed a treadmill gait trial with 20% body-weight support for approx. 1 min. The outcome data during the BWS training were from five gait cycles at from 25 sec to 35 sec after the start of the treadmill gait. The long-term effects of the BWS training were assessed by EMG and fMRI at 3 weeks (3 weeks) and 4 weeks (Follow-up) after the first day of the training. In the evaluation sessions, no AFO was used.

The patient also underwent conventional physical therapy (including overground gait training and ADL training) plus occupational therapy (i.e., training of the right upper arm using a hand-ergometer and ADL training) throughout the training period. He used a metal double-upright AFO on his right lower extremity. The AFO has two Klenzak joints set at 0° with plantarflexion rod stops and at 20° with dorsiflexion rod stops. There were no medication changes affecting the relief of the patient's muscle tonus during the BWS training or during the patient's evaluation for this report.

Outcome

Step lengths of the patient's paretic foot and nonparetic foot

For the spatial quantification of the patient's gait, we performed a step-length analysis using a video camera (frame rate: 60 Hz; HDR-CX 470, Sony Marketing, Tokyo) and analysis software (Kinovea, ver. 0.8.26). Gait event detection was performed using videographic techniques with visual detection[11]. Visual detection was performed by direct observation of the video, without using any tools from the software. For event detection, the rater reported the video frame in which the foot first made contact with the floor after the swing phase (Initial contact), and the first instant of foot-off from the floor after the stance phase (Foot-off).

For step length analysis, the paretic step length ($SL_{paretic}$) (in cm) was defined as the distance between anterior-posterior positions (Fig. 3A; the walking direction is presented as a positive value) from the nonparetic initial contacts to the paretic initial contacts. The nonparetic step length ($SL_{nonparetic}$) was defined as the distance between anterior-posterior positions from the paretic initial contacts to the nonparetic initial contacts (Fig. 3B). When the patient's nonparetic leg could not overtake the paretic leg, the nonparetic step length was negative (Fig. 3C). The $SL_{paretic}$ and $SL_{nonparetic}$ values were measured for five consecutive gait cycles.

Step-length asymmetry in the gait ($SL_{asymmetry}$) was defined as $100\% \times (SL_{paretic} - SL_{nonparetic})/(SL_{paretic} + SL_{nonparetic})$ for each walking cycle. An index of 0% indicates perfect symmetry; the magnitude represents the degree of asymmetry, and the sign indicates the direction of the asymmetry. That is, a positive index indicates a larger step length for the paretic leg during the paretic step. The mean and standard deviation of the $SL_{paretic}$, $SL_{nonparetic}$, and $SL_{asymmetry}$ values were

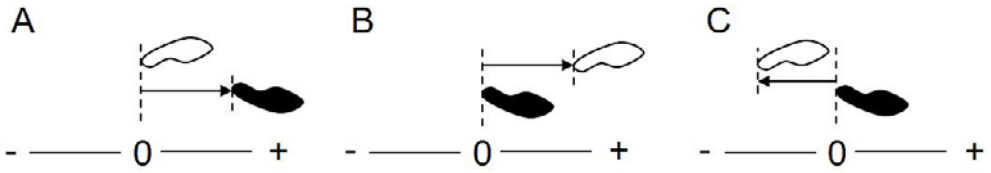

Fig. 3. Analysis of the step length. The filled foot represents the paretic side. The walking direction is shown as positive. **A:** The paretic step length (*arrow*). **B:** The nonparetic step length (*arrow*). **C:** When the nonparetic leg could not overtake the paretic leg, the nonparetic step length is shown as negative (*arrow*).

calculated.

EMG

We performed EMG measurements of the patient's gastrocnemius medialis (GM) muscle on both sides (Lt-GM, Rt-GM) and tibialis anterior (TA) muscle on both sides (Lt-TA, Rt-TA) by using a surface EMG device (Trigno Wireless Systems, Delsys, MA). These muscles were chosen as the representative ankle muscles that are mainly responsible for plantarflexion and dorsiflexion. Electrodes were located on the skin according to SENIAM recommendations[12]. The recording sites were cleaned with an alcohol solution and allowed to dry. The EMG signals were collected at a sampling rate of 2,000 Hz with 20-450 Hz bandpass filtering. The absolute EMG was integrated by time in order to calculate the integrated EMG (iEMG) in 100 msec.

EMG patterns at the maximum voluntary contraction (MVC) of the TA and GM muscles were recorded for $\geq$5 sec at the first day and 3 weeks of the intervention, and at follow-up. Using visual inspection, the smallest variation of a 2-sec EMG segment was selected and averaged for 2 sec (100% MVC). The iEMG data during movement were divided by the 100% MVC value (recorded each day) to calculate the %MVC data. The method using the 2-sec MVC data was described previously[13].

The EMG signals were processed using MATLAB R 2019b software (MathWorks, Natick, MA). To standardize the time of one gait cycle as 100%, all of the data were interpolated and smoothed by the fourth-order Butterworth filter. One gait cycle was defined as the sequence of events between two sequential initial contacts.

For the TA muscle iEMG, the peak timing (% gait cycle) and the peak amplitude on five gait cycles under each condition were analyzed. The mean value and standard deviation were calculated under each condition.

Functional MRI

For the assessment of the cortical activation by the voluntary movement of the patient's lower extremity muscles, echo planar fMRI was performed using a 1.5T MRI system (EXCELART Vantage, Toshiba, Tokyo). For echo planar imaging, the sequence was as follows: TR = 3000 msec, TE = 40 msec, flip angle = 80°, number of slices = 32, slice thickness = 3.2 mm, matrix = 64 × 64, voxel size = 3.4 mm^2, total time = 5 min. The run began with three dummy volumes to allow for T1 equilibration effects; these volumes were subsequently discarded. The patient was scanned during the performance of two tasks that were performed based on a block design (task 30 sec, rest 30 sec); each task involved a different movement (right foot dorsiflexion, left foot dorsiflexion). Each task was performed in five blocks interspersed with rest blocks.

The image processing and statistical analysis were performed using the SPM12 program (ver. r7487; Wellcome Department of Cognitive Neurology, London, UK). First, to correct for dislocations caused by head motion, all images were realigned. The realigned images were then normalized to the Montreal Neurological Institute template brain supplied with SPM 12. Finally, the images were smoothed using an 8-mm Gaussian kernel.

Statistical analysis

The effects of BWS treadmill training on the patient's step length and the asymmetry on the days of the training period were assessed with a one-way repeated measures analysis of variance (ANOVA) with the time (Pre-BWS, Inter-BWS, Post-BWS) as a within-subject factor. Bonferroni's correction was used for post hoc comparisons when the ANOVA revealed significant differences. The level of statistical significance was set at $p<0.05$.

For the iEMG and %gait cycle of the EMG peak amplitude data, we conducted a one-way ANOVA with the time (Pre-BWS, Inter-BWS, Post-BWS or the first day of the intervention, 3 weeks, or follow-up) as a within-subject factor. Holm's correction was used for post hoc comparisons when the ANOVA revealed significant differences. When two peaks were observed in a single gait cycle, they were analyzed separately at the stance phase (during initial contact to foot-off) and swing phase (during foot-off to the next initial contact). The data were analyzed using R (ver. 2.8.1), a language and environment for statistical computing and graphics (http://cran.r-project.org/).

For the fMRI, a general linear model (GLM) analysis was performed to obtain average brain responses associated with the task. Regions of interest (ROIs) in the left hemisphere and their right hemispheric homologues were created using the Neuromorphometrics atlas of the sensory-

Fig. 4. Examples of the nonparetic step length on the first day of the training period. **A:** Pre-BWS. **B:** Inter-BWS. **C:** Post-BWS.

Table 1. Step length and asymmetry on the first day of the training period

	Pre-BWS	Inter-BWS	Post-BWS
$SL_{nonparetic}$, cm	−16.2 (0.7)	6.8 (2.8)*	−12.0 (1.4)*†
$SL_{paretic}$, cm	48.7 (1.3)	21.7 (1.1)*	43.9 (2.9)†
$SL_{asymmetry}$, %	200.1 (9.6)	53.3 (16.6)*	175.3 (9.7)*†

Values are mean (SD). *p<0.05 vs. Pre-BWS. †p<0.05 vs. Inter-BWS.
$SL_{nonparetic}$: Nonparetic step length. $SL_{paretic}$: Paretic step length. $SL_{asymmetry}$: Step length asymmetry, defined as $100\% \times (SL_{paretic} - SL_{nonparetic})/(SL_{paretic} + SL_{nonparetic})$.

motor area (precentral cortex, postcentral cortex, supplementary motor area, superior parietal lobe, supramarginal cortex, and angular gyrus). The numbers of activated voxels (showing activation above a threshold of $p < 0.05$, family-wise error [FWE] corrected) were counted in the ROIs in each hemisphere.

Results

On the first day of the intervention, the patient reported feeling fatigue (Borg scale: 12), and the intervention was discontinued after 12 min. The second and third intervention periods were each 18 min. The duration of the 4th to 14th interventions was 20 min.

The step lengths of the patient's paretic foot and nonparetic foot

Based on the results of the one-way repeated measures ANOVA for the $SL_{nonparetic}$ data, a main effect was observed for the difference in the time ($F(2, 12) = 221.27$, $p<0.001$) (Fig. 4, Table 1). In the Bonferroni correction, the $SL_{nonparetic}$ value at the Inter-BWS period was significantly larger than those of the Pre-BWS and Post-BWS periods (both $p<0.001$). The $SL_{nonparetic}$ value at the Post-BWS period was significantly larger than that at the Pre-BWS period ($p=0.025$; Fig. 4, Table 1). The one-way repeated measures ANOVA for the $SL_{paretic}$ data revealed a main effect for the difference in the time ($F(2, 12) = 275.36$, $p<0.001$) (Table 1). In the Bonferroni correction, the $SL_{paretic}$ at Inter-BWS was significantly smaller than those at the Pre-BWS ($p<0.001$) and Post-BWS ($p<0.001$) periods (Table 1).

The one-way repeated measures ANOVA for $SL_{asymmetry}$ showed a main effect of the difference in the time ($F(2, 12) = 200.27$, $p<0.001$) (Table 1), and in the Bonferroni correction, the $SL_{asymmetry}$ at Inter-BWS was significantly smaller than those at the Pre-BWS ($p<0.001$) and Post-BWS ($p<0.001$) periods. The $SL_{asymmetry}$ at Post-BWS was significantly larger than that at Pre-BWS ($p=0.033$) (Table 1).

EMG

In the iEMG of the patient's Rt-GM muscle in the stance phase, the EMG activity at Inter-BWS was lower than that at Pre-BWS (Fig. 5). The EMG activity at Post-BWS was higher than that at Pre-BWS. The iEMG of the Rt-GM muscle at Pre-BWS exhibited a peak at the right swing phase (Fig. 5). This signal was gradually decreased throughout the sessions (Pre-BWS > Inter-BWS > Post-BWS session). This signal was also decreased at 3 weeks after the first day of the training and during the follow-up session.

At the peak amplitude of the iEMG on the first day of the intervention, the results of the one-way repeated measures ANOVA for the Rt-TA muscle revealed no main effect of time ($F(2, 12) = 0.51$, $p=0.61$) (Fig. 6, Table 2). Regarding the results of the Lt-TA stance phase, there was a main effect of time ($F(2, 12) = 15.1$, $p<0.001$). In the Holm correction, the peak amplitude of the iEMG in the Lt-TA stance phase of Inter-BWS became significantly smaller than that observed at Pre-BWS ($p<0.001$). Similarly, the peak amplitude of the iEMG in the Lt-TA stance phase Post-BWS became significantly larger than that at the Inter-BWS period ($p<0.001$). In the Lt-TA swing phase results,

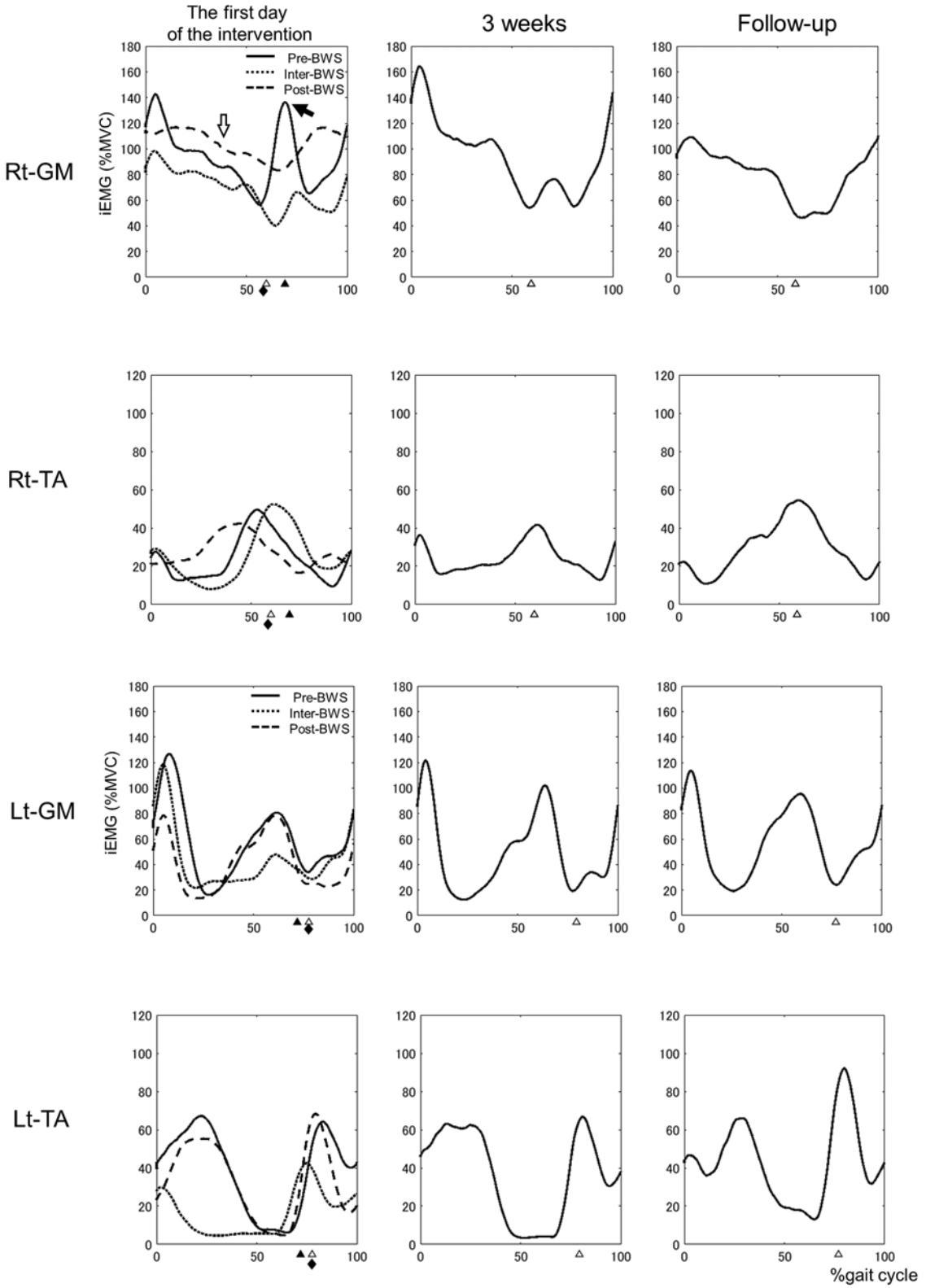

Fig. 5. Integrated electromyographic (iEMG) results of the gastrocnemius medialis (GM) muscle and tibialis anterior (TA) muscle on the first day of the intervention, at 3 weeks, and at follow-up. *White arrow*: The right (Rt)-GM muscle during the mid-stance phase on the first day of the intervention. *Black arrow*: A peak of the right swing phase in the Rt-GM at Pre-BWS on the first day of the intervention. *Solid line*: Pre-BWS session. *Dotted line*: Inter-BWS session. *Dashed line*: Post-BWS session. %MVC: %muscle voluntary contraction. The timings of foot-off are indicated with *white triangles* for the Pre-BWS, *filled triangles* for the Inter-BWS, and *diamond symbols* for the Post-BWS session.

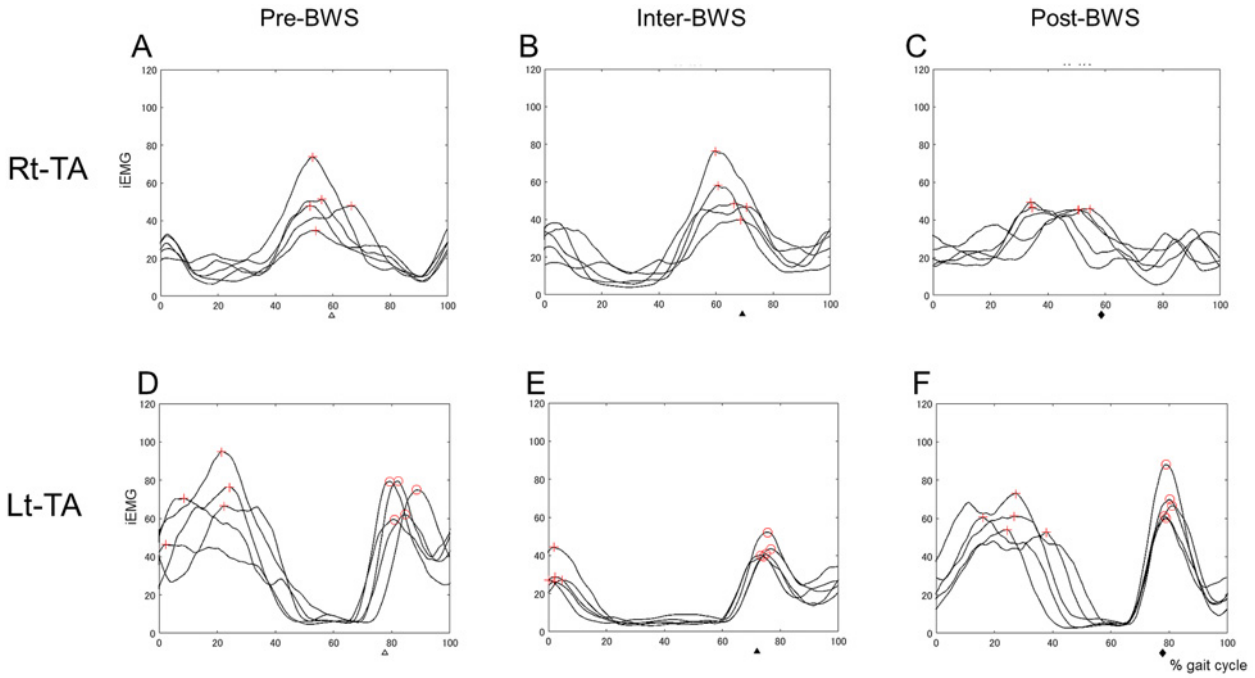

Fig. 6. The iEMG of five gait cycles of the right and left TA muscles on the first day of the intervention. The peak amplitude of the TA is indicated with *crosses* or *circles*. **A, D:** Pre-BWS session. **B, E:** Inter-BWS session. **C, F:** Post-BWS session. The timings of foot-off are indicated with *white triangles* for the Pre-BWS, *filled triangles* for the Inter-BWS, and *diamond symbols* for the Post-BWS session.

Table 2. Peak amplitude and peak timing on integrated electromyography (iEMG) of the tibialis anterior (TA) muscles on the first day of intervention

		Pre-BWS	Inter-BWS	Post-BWS
Rt-TA	iEMG (%MVC)	51.3 (14.2)	53.9 (14.1)	46.6 (1.6)
	%gait cycle	56.3 (5.8)	65.2 (4.8)	44.8 (9.8)†
Lt-TA stance	iEMG (%MVC)	71.0 (17.6)	30.6 (7.7)*	60.4 (8.0)†
	%gait cycle	15.8 (9.7)	2.2 (1.6)*	26.5 (7.8)*†
Lt-TA swing	iEMG (%MVC)	71.0 (9.6)	43.1 (5.3)*	69.2 (11.3)†
	%gait cycle	83.1 (3.6)	74.9 (1.4)*	79.4 (1.1)*†

Values are mean (SD). *p<0.05 vs. Pre-BWS. †p<0.05 vs. Inter-BWS.

there was a main effect of time ($F(2, 12) = 14.6$, $p<0.001$). The use of the Holm correction showed that the peak amplitude of the iEMG in the Lt-TA swing phase at Inter-BWS became significantly smaller than that at Pre-BWS ($p=0.001$). Similarly, the peak amplitude of the iEMG in the Lt-TA swing phase of the Post-BWS period became significantly larger than that at Inter-BWS ($p=0.001$).

At the peak timing of the iEMG on the first day of the intervention, regarding the results of the Rt-TA muscle, there was a main effect of time ($F(2, 12) = 10.16$, $p=0.003$) (Fig. 6, Table 2). In the Holm correction, the peak timing of the iEMG in the Rt-TA muscle of the Post-BWS period became significantly earlier than that at Inter-BWS ($p=0.002$). For the Lt-TA stance phase results, there was a main effect of time ($F(2, 12) = 14.2$, $p<0.001$). With the Holm correction, the peak timing of the iEMG in the Lt-TA stance phase of Inter-BWS became significantly earlier than that at Pre-BWS ($p=0.023$). Similarly, the peak timing of the iEMG in the Lt-TA stance phase Post-BWS became significantly later than that at Inter-BWS ($p<0.001$). Concerning the results of the Lt-TA swing phase, there was a main effect of time ($F(2, 12) = 15.6$, $p<0.001$). With the Holm correction, the peak timing of the iEMG in the Lt-TA swing phase at Inter-BWS became significantly earlier than that at Pre-BWS ($p<0.001$). Similarly, the peak timing of the iEMG in the Lt-TA swing phase at Post-BWS became significantly later than that at Inter-BWS ($p=0.019$).

At the peak amplitude of the iEMG on the first day of the intervention, at 3 weeks, and at the Follow-up, the results of the one-way repeated measures ANOVA for the Rt-TA muscle showed no main effect ($F(2, 12) = 2.7$, $p=0.11$) (Fig. 7, Table 3). In the Lt-TA stance phase results, no main effect of time was observed ($F(2, 12) < 0.1$, $p=0.94$), whereas in the results of the Lt-TA swing phase, there was

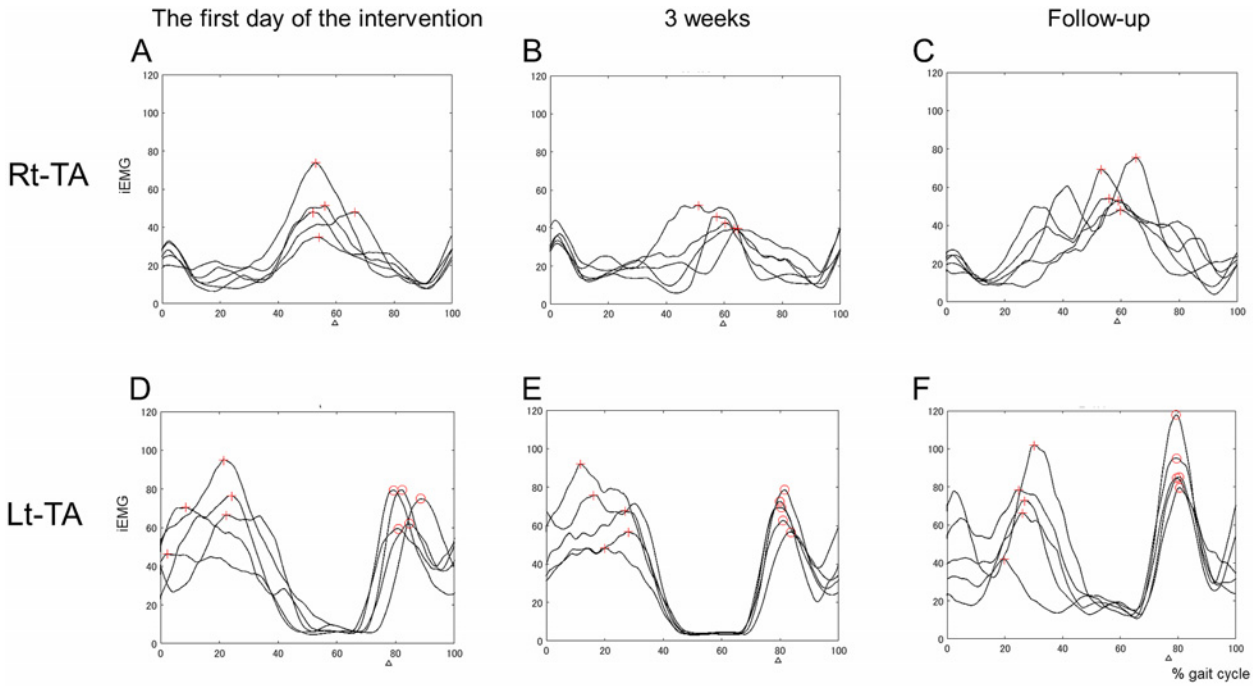

Fig. 7. The iEMG of five gait cycles of the right and left TA muscles on the first day of the intervention, at 3 weeks, and at follow-up. Peak amplitudes of the TA are shown as *crosses or circles*. **A, D:** The first day of the intervention. **B, E:** 3 weeks after the first day of the intervention. **C, F:** follow-up. The timings of foot-off are indicated with *white triangles*.

Table 3. Peak amplitude and peak timing on integrated electromyography (iEMG) of the TA muscles on the first day of intervention, at 3 weeks, and at follow-up

		First day of intervention	3 weeks	Follow-up
Rt-TA	iEMG (%MVC)	51.3 (14.2)	44.0 (5.2)	60.1 (11.8)
	%gait cycle	56.3 (5.8)	59.4 (5.4)	58.6 (4.5)
Lt-TA stance	iEMG (%MVC)	71.0 (17.6)	68.1 (17.0)	72.3 (21.7)
	%gait cycle	15.8 (9.7)	20.6 (7.0)	25.6 (3.8)
Lt-TA swing	iEMG (%MVC)	71.0 (9.6)	67.9 (8.5)	92.4 (15.2)*†
	%gait cycle	83.1 (3.6)	81.3 (1.5)	79.8 (0.6)

Values are mean (SD). *p<0.05 vs. the first day of the intervention. †p<0.05 vs. 3 weeks.

a main effect of time ($F(2, 12) = 6.7$, $p=0.01$). With Holm's correction, the peak amplitude of the iEMG in the Lt-TA swing phase of the Follow-up became significantly larger than those at Pre-BWS ($p=0.03$) and 3 weeks ($p=0.02$).

At the peak timing of the iEMG on the first day of the intervention, at 3 weeks, and at the Follow-up, the results of the one-way repeated measures ANOVA for the Rt-TA muscle showed no main effect ($F(2, 12) = 0.5$, $p=0.64$) (Fig. 7, Table 3). In the Lt-TA stance phase results, there was no main effect of time ($F(2, 12) <2.3$, $p=0.14$), and in the results for the Lt-TA swing phase, there was also no main effect of time ($F(2, 12) <2.6$, $p=0.11$).

Functional MRI

For both the left and right dorsiflexion tasks, not only the lower-limb representation area of the motor cortex but also other areas (the left and right precentral cortex, left and right postcentral cortex, left and right supplementary motor area, left and right superior parietal lobe, left and right supramarginal cortex, and right angular gyrus) were activated at Pre-BWS (Fig. 8, Table 4). The total voxel count decreased throughout the study period: Pre-BWS > 3 weeks > Follow-up (Fig. 8, Table 4).

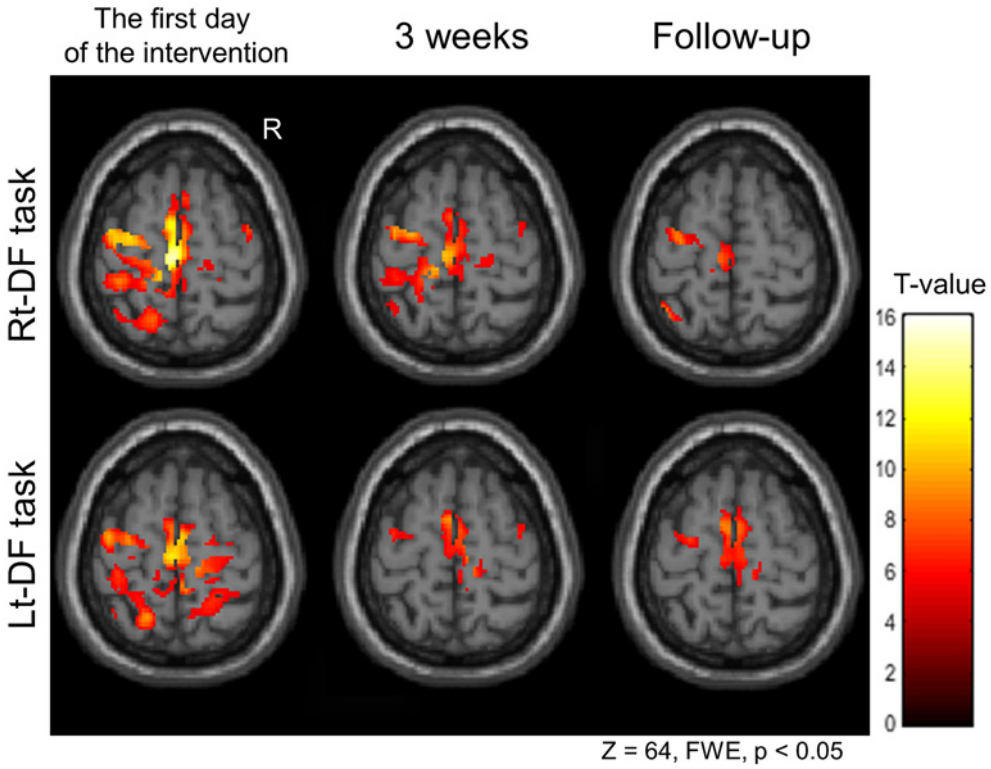

Fig. 8. Cortical activation by the left or right dorsiflexion task on the first day of the intervention, at 3 weeks, and at follow-up. The images at Z=64 mm above the anterior-posterior commissural plane are shown. The *left side* of the figure corresponds to the left "lesioned" hemisphere. The statistical threshold was set to the FWE-corrected p-value <0.05. Rt-DF: right dorsiflexion; Lt-DF: left dorsiflexion.

Table 4. Voxel counts of the cortical activation by the left and right dorsiflexion tasks in the ROIs on the first day of the intervention, at 3 weeks, and at follow-up

	Hemisphere	Baseline	3 weeks	Follow-up
Rt-DF task	Left	5,806	2,109	1,023
	Right	958	1,073	373
Lt-DF task	Left	2,414	811	885
	Right	1,570	1,082	811

Voxels counts were calculated above the statistical threshold that was set to the FWE-error-corrected p-value <0.05. Rt-DF: right dorsiflexion. Lt-DF: left dorsiflexion.

Discussion

Our findings for this patient with post-stroke hemidystonia demonstrated that (1) the patient's gait pattern was modified immediately after the BWS treadmill training, and the modification pattern was maintained to the follow-up period; and (2) there was a change in the cortical activation in the sensory-motor area evoked by the voluntary movement after the BWS intervention period.

The iEMG of the patient's Rt-GM muscle in the right mid-stance phase at Inter-BWS was decreased compared to that at Pre-BWS on the first day of the intervention. This result indicates that the patient's excessive muscle activities for gait were suppressed by the body weight support that we provided. The step-length analysis revealed a significant extension of the nonparetic step length at Inter-BWS compared to the Pre-BWS session, suggesting an extension of the paretic stance phase. In addition, the patient's gait symmetry was improved at Inter-BWS compared to the Pre-BWS session. These results suggest that the body weight support reduced the patient's symptoms of post-stroke hemidystonia in his lower extremities.

Moreover, the significant extension of the patient's nonparetic step length and the improvement of his gait

symmetry lasted until the Post-BWS session. The iEMG of the Rt-GM in the right mid-stance phase at Post-BWS was increased compared to that at Pre-BWS. In healthy subjects, the GM muscle must push off the ground in the stance phase[14]. The reason why the iEMG of the patient's Rt-GM in the right mid-stance phase at Post-BWS was increased compared to that at Pre-BWS on the first day of the intervention is unclear, because we did not measure the data of the trajectory of the center of gravity and the left-right ratio of the stance time. Presumably, the increase in the iEMG of the patient's Rt-GM muscle during the mid-stance phase of the post-BWS compared to the pre-BWS was due to the increased weight bearing of the right lower limb and the increased activity of the Rt-GM (which is the antigravity muscle) as a result of the increased shift of the center of gravity toward the right side in the right stance phase.

In healthy subjects, there is no activity of the GM muscle in the swing phase[14]. Jung et al.[15] reported excessive GM muscle activity in a dystonia patient. In our patient, excessive Rt-GM muscle activity was observed at the Pre-BWS session. These results suggest that excessive GM activity in the right swing phase is one of the characteristics of post-stroke hemidystonia. Our patient's excessive Rt-GM activity in the right swing phase was decreased at the Inter-BWS, Post-BWS, the 3-week time point, and the follow-up period compared to that at the Pre-BWS session, indicating that the BWS intervention improved the EMG activity pattern in the right swing phase.

The iEMG findings of the TA muscles in our patient demonstrated that the BWS training resulted in a change in the peak amplitude and timing on the first day of intervention. These changes did not occur steadily across time from the start to the end of the training period. These results imply that the carry-over effect of the TA muscle is not obtained before or after training.

Dystonic movements are associated not only with the cortico-basal-ganglia and cerebello-cortical motor network[7,16] but also with overactivation in the sensorimotor cortex[17]. Our patient's fMRI results showed that the cortical areas activated by a motor task of left or right dorsiflexion were converged, which suggests that the converged fMRI activation patterns were related to the symptom improvement in this patient. Previous studies have shown that neural-activity convergence is caused by the progression of motor learning[18,19], which suggests that our patient's excessive Rt-GM muscle activity was decreased through motor learning.

Several limitations of this study should be noted. First, the patient presented with motor and sensory impairments. Due to these impairments, the MVC measurement could not be performed stably. At the time of MVC measurement, an increase in the amplitude of myoelectric activity was observed, and the patient was able to exert some muscle strength. However, the activity of the GM muscles during gait exceeded 100% MVC. In previous reports on MVC in stroke patients, torque-measurement sensors were used to evaluate the accuracy of MVC measurements[20,21]. In our present study, however, we did not measure torque, and thus the accuracy of the MVC value could not be verified. Therefore, the low reliability of the %MVC data is one of the limitations to the interpretation of EMG in this study. Second, we analyzed the EMG data during the BWS training from 25 sec to 35 sec after the start of the treadmill gait. Over this interval, no muscle fatigue was expected in this patient. Meyer et al.[22] reported that healthy adults' familiarization with treadmill walking requires 6 minutes; this finding indicates that our analysis time window was not long enough for the patient to become familiar with treadmill walking. These factors should be taken into consideration when interpreting the results of EMG data during BWS training. Third, we identified walking events using a video camera. Peterson et al.[11] reported that there was an average difference of 60 ms between the identification of walking events using a video camera and the identification of walking events using the floor reaction force, and thus that the video camera was highly reliable for identifying walking events. Moreover, Peterson et al. used a video camera with a sampling frequency of 30 Hz, whereas our video camera had a sampling frequency of 60 Hz. Due to this higher time resolution, our analysis would have been more accurate than that of Peterson et al. Nonetheless, because we did not measure the floor reaction force or foot pressure using sensors, the accuracy of the identification of walking events in our study could not be verified. Fourth, the task used in the fMRI examination was ankle dorsiflexion movement, which is affected mainly by the portion of the primary motor area where the lower limbs are represented. In our patient, not only the muscles of the right lower extremity but also those of the right upper extremity were overactive due to dystonia. In the ankle dorsiflexion movement, activation was observed not only in the areas represented by the lower limbs in the primary motor area, but also across a wider region. In addition, the patient was undergoing arm training using a hand-ergometer as occupational therapy. These results suggest that the changes in brain activity that occurred in his case may have included effects other than those due to the BWS intervention.

Conclusion

Our patient with a chronic-stage thalamic hemorrhage performed 14 sessions of BWS treadmill training over a 3-week period. The patient's gait pattern was modified immediately after the BWS treadmill training, and the modification pattern was maintained through the follow-up period. There was a change in the cortical activation in the sensorymotor area evoked by the voluntary movement after the BWS intervention period. These results suggest that there

was improvement of the symptoms of post-stroke hemidystonia due to changes in the brain activity during voluntary movement after the BWS intervention. Body weight-supported treadmill training may thus be an effective treatment for patients with post-stroke hemidystonia.

Conflict of Interest: The authors state that they have no conflicts of interest to disclose.

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